DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

ONE HUNDRED TWENTY SIXTH REGULAR MEETING OF THE
NATIONAL ADVISORY ENVIRONMENTAL HEALTH SCIENCES COUNCIL
February 19, 2009
BUILDING 101, RODBELL AUDITORIUM
NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
RESEARCH TRIANGLE PARK, NORTH CAROLINA
CONTACT PHONE: (919) 541-0132

AGENDA

OPEN SESSION – February 19th, 2009 – 8:30 am

8:30	**I.**	**Call to Order and Opening Remarks**	**Dr. Linda Birnbaum**
	II.	**Review of Confidentiality and Conflict of Interest**	**Dr. Gwen Collman**
	III.	**Consideration of September 2008 Meeting Minutes**	**Dr. Gwen Collman**
8:45	**IV.**	**Report of the Director, NIEHS**	**Dr. Linda Birnbaum**
9:15	**V.**	**Discussion of Director's Report**	
10:15	**Break**		
10:30	**VI .**	**Report of the Director, DIR**	**Dr. Steve Akiyama**
10:45	**VII.**	**Report of the Director, NTP**	**Dr. John Bucher**
11:00	**X.**	**Report of the Editor-in-Chief**	**Dr. Hugh Tilson**
11:15	**XI.**	**Report of the Acting Director, DERT**	**Dr. Gwen Collman**
12:00		**Lunch**	
1:00	**XII.**	**Update on Exposure Biology**	**Dr. David Balshaw**
1:30	**XIII.**	**Superfund Presentation**	**Dr. Claudia Thompson** **Mr. Chip Hughes**
2:00	**XIV.**	**Concept Clearance – Virtual Consortium for Transdisciplinary/Translational Envrionmental Research (VicTTer)**	**Dr. Jerry Heindel**

CLOSED SESSION [1] –

2:30 XV. Consideration of Grant Applications — **Dr. Gwen Collman and DERT staff**

5:00 XVI. Adjournment of the NAEHS Council

FUTURE MEETING DATES

May 21-22, 2009	**NIEHS**
September 14-16, 2009	**NIEHS**
February 17-19, 2010	**NIEHS**
May 19-20, 2010	**NIEHS**

[1]This portion of the meeting is being closed to the public in accordance with the provisions set forth in Section 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

SEATING CHART

NATIONAL ADVISORY ENVIRONMENTAL HEALTH SCIENCES COUNCIL
February 19, 2009
National Institute of Environmental Health Sciences
Research Triangle Park, North Carolina

Ms. Michelle Owens Dr. Gwen Collman Dr. Linda Birnbaum

Ms. Liz McNair
Dr. David Christiani
Ms. Stefani Hines
Dr. Dan Liebler
Dr. Altaf Wani
Dr. Richard Finnell
Dr. John Essigmann
Dr. Kevin Stephens
Dr. Kenneth Ramos
Dr. Grace LeMasters
Ms. Janet McCabe
Dr. Sem Phan

Dr. John Bucher
Dr. Steve Akiyama
Mr. Marc Hollander
Dr. George Leikauf
Dr. Hillary Carpenter
Dr. Joe Graziano
CPT Michael Macinski
Dr. Jerald Schnoor
Dr. Stephen Lloyd
Dr. Palmer Taylor
Dr. Nsedu Obot Witherspoon

Report to the National Advisory Environmental Health Sciences Council
Director, NIEHS
February 19, 2009

Dr. Linda Birnbaum entered on duty as Director, National Institute of Environmental Health Sciences, on January 18, 2009.

Director's Message

It is my pleasure and privilege to address you on the occasion of my initial meeting with the National Advisory Environmental Health Sciences Council. I am proud to be entrusted with the leadership of this great institute, and I am hoping that with your help and with the efforts of all of us – our top notch scientists and staff, and our outstanding extramural community – we can move beyond the turbulence of the recent past and advance our mission at a time in scientific history that has never been more exciting and full of promise.

The challenges to the field of environmental health sciences in the 21st century are enormous. As biological sciences generate a deeper understanding of the working of organisms at the molecular and systems levels, so opportunities open for us to advance our knowledge of the effects of environmental exposures and to understand both the robust and the subtle, complex ways in which exposures affect human health and disease. Tackling scientific questions with this level of complexity will require an ongoing evaluation of our ideas and approaches and an emphasis on integration across disciplines: computational and molecular to clinical and public health, and everything in between. We also have a responsibility as an institute to empower efforts to translate our discoveries into improvements in public health and clinical practice.

Over the coming months, I will be emphasizing "evolution, not revolution", as I come up to speed regarding my knowledge of current NIEHS programs, organization, and issues. I am eager to have the Council's advice and input as we move forward. I view the Council as an invaluable resource, with a wealth of knowledge both about the NIEHS and about the state of environmental health sciences in general, and also as an outside point of view with which to compare and check my own impressions. I hope to be able to have an open, honest dialog with this group, and will always welcome your opinions and insight.

I also want to extend my deep appreciation, for myself and on behalf of the entire NIEHS community, to Drs. Sam Wilson and Bill Suk for their leadership of NIEHS over the past seventeen months.

Recent Scientific Advances

1. Pope CA 3rd, Ezzati M, Dockery DW. Fine-particulate air pollution and life expectancy in the United States. N Engl J Med. 2009 Jan 22;360(4):376-86. HTML PDF

2. Navas-Acien A, Silbergeld EK, Pastor-Barriuso R, Guallar E. Arsenic exposure and prevalence of type 2 diabetes in US adults. JAMA. 2008 Aug 20;300(7):814-22. HTML PDF

3. Stevens RC, Suzuki SM, Cole TB, Park SS, Richter RJ, Furlong CE. Engineered recombinant human paraoxonase 1 (rHuPON1) purified from *Escherichia coli* protects against organophosphate poisoning. Proc Natl Acad Sci U S A. 2008 Sep 2;105(35):12780-4. HTML PDF

4. Chuang KJ, Coull BA, Zanobetti A, Suh H, Schwartz J, Stone PH, Litonjua A, Speizer FE, Gold DR. Particulate air pollution as a risk factor for ST-segment depression in patients with coronary artery disease. Circulation. 2008 Sep 23;118(13):1314-20. HTML PDF

5. Chou AP, Maidment N, Klintenberg R, Casida JE, Li S, Fitzmaurice AG, Fernagut PO, Mortazavi F, Chesselet MF, Bronstein JM. Ziram causes dopaminergic cell damage by inhibiting E1 ligase of the proteasome. J Biol Chem. 2008 Dec 12;283(50):34696-703. HTML PDF

6. Straub AC, Clark KA, Ross MA, Chandra AG, Li S, Gao X, Pagano PJ, Stolz DB, Barchowsky A. Arsenic-stimulated liver sinusoidal capillarization in mice requires NADPH oxidase-generated superoxide. J Clin Invest. 2008 Dec;118(12):3980-9. HTML PDF

7. Williams MA, Rangasamy T, Bauer SM, Killedar S, Karp M, Kensler TW, Yamamoto M, Breysse P, Biswal S, Georas SN. Disruption of the transcription factor Nrf2 promotes pro-oxidative dendritic cells that stimulate Th2-like immunoresponsiveness upon activation by ambient particulate matter. J Immunol. 2008 Oct 1;181(7):4545-59. HTML PDF

8. Waalkes MP, Liu J, Germolec DR, Trempus CS, Cannon RE, Tokar EJ, Tennant RW, Ward JM, Diwan BA. Arsenic exposure in utero exacerbates skin cancer response in adulthood with contemporaneous distortion of tumor stem cell dynamics. Cancer Res. 2008 Oct 15;68(20):8278-85. HTML PDF

9. Hartz AM, Bauer B, Block ML, Hong JS, Miller DS. Diesel exhaust particles induce oxidative stress, proinflammatory signaling, and P-glycoprotein up-regulation at the blood-brain barrier. FASEB J. 2008 Aug;22(8):2723-33. HTML PDF

10. Donohue KM, Al-alem U, Perzanowski MS, Chew GL, Johnson A, Divjan A, Kelvin EA, Hoepner LA, Perera FP, Miller RL. Anti-cockroach and anti-mouse IgE are associated with early wheeze and atopy in an inner-city birth cohort. J Allergy Clin Immunol. 2008 Nov;122(5):914-20. HTML PDF

11. Brown KH, Schultz IR, Cloud JG, Nagler JJ. Aneuploid sperm formation in rainbow trout exposed to the environmental estrogen 17{alpha}-ethynylestradiol. Proc Natl Acad Sci U S A. 2008 Dec 16;105(50):19786-91. HTML PDF

12. Wallace K, Kelsey KT, Schned A, Morris JS, Andrew AS, Karagas MR. Selenium and risk of bladder cancer: a population-based case-control study. Cancer Prev Res (Phila Pa). 2009 Jan;2(1):70-3. HTML PDF

13. Perera F, Li TY, Zhou ZJ, Yuan T, Chen YH, Qu L, Rauh VA, Zhang Y, Tang D. Benefits of reducing prenatal exposure to coal-burning pollutants to children's neurodevelopment in China. Environ Health Perspect. 2008 Oct;116(10):1396-400. HTML PDF

14. Garantziotis S, Li Z, Potts EN, Kimata K, Zhuo L, Morgan DL, Savani RC, Noble PW, Foster WM, Schwartz DA, Hollingsworth JW. Hyaluronan mediates ozone-induced airway hyperresponsiveness in mice. J Biol Chem. 2009 Jan 21. [Epub ahead of print] PDF

Institute Highlights and Milestones

- "Genetic Susceptibility to Air Pollution Outcome Models: Approaches to Translation of Cariopulmonary Animal Disease Models," workshop focused on improving research related to susceptibility to respiratory and cardiovascular outcomes, held at NIEHS Sept. 4-5, 2008.
- Cincinnati Town Meeting: "Your Home, Your Health, Your Voice," hosted by NIEHS and University of Cincinnati, Sept. 15, 2008.
- NIEHS, with NIDA, NIDDK, and OPASI, announced Sept. 29, 2008, funding for the new NIH Roadmap Epigenomics Program that will invest more than $190 million over the next five years to accelerate this emerging field of biomedical research.
- NIEHS announced on Sept. 16, 2008, that it will award three new grants totaling $21.25 million over a five-year period to study how environmental factors contribute to the cause, prevention and treatment of Parkinson's Disease and related disorders.
- NIEHS chaired organizing committee and co-chaired workshop: "Environmental risks of respiratory disease". Indo-US Joint Working Group on Environment and Occupational Health. Chandigarh, India. September, 2008 (Co-sponsored by NIEHS, NICHD, CDC, EPA, American Thoracic Society, Health Effects Institute and the Indian Council for Medical Research)
- NIEHS organized and chaired workshop in Bethesda MD (NIH campus) entitled "Environmental Systems of Public Health" cosponsored by NIEHS, NICHD, OBSSR and NCI. September 2008.
- NIEHS co-sponsored International Environmental Nanotechnology Conference: Applications and Implications was cosponsored by the NIEHS Superfund Basic Research Program, Oct. 7-9, 2008.
- Implications for Safety and Health Training in a Green Economy, a workshop sponsored by the NIEHS Worker Education and Training Program, Oct. 16-17, 2008.
- Central and Eastern European Conference on Health and the Environment: The Environment – A Platform for Health, a workshop cosponsored by the NIEHS Superfund Basic Research Program, Oct. 19-22, 2008, in Cluj-Napoca, Romania.
- P30 Core Center Director's Meeting, Oct. 19-21, 2008, a meeting of the leadership of the twenty Environmental Health Sciences Core Centers from around the nation, to discuss

gene-environment interactions with regard to emerging research, disease risk, and public health.

- Dioxin Toxicity: Mechanisms, Models, and Potential Health Risks, a NIEHS SBRP cosponsored event, Oct. 20-21, at Michigan State University.
- 5th Annual Early Exposures Meeting, a conference on the emerging topics in breast cancer and the environment research conducted at NIEHS co-sponsored centers, Nov. 13-14, 2008, in Birmingham, Alabama.
- Expert Panel on Cobalt-Tungsten Carbide Powders and Hardmetal, Dec. 9-10, 2008, in Chapel Hill, provided a National Toxicology Program forum open to public comment, regarding whether these metals should be listed in the 12th Report on Carcinogens.
- Samuel Wilson, M.D., and Jerry Yakel, Ph.D., senior scientists at NIEHS, were named 2008 Fellows by the American Association for the Advancement of Sciences at their annual meeting in December.
- The NTP Board of Scientific Counselors met Nov. 20, 2008, and voted to accept three working group reports on the establishment of new criteria for future NTP immunotoxicology, reproductive, and developmental studies. The criteria are similar to those used with the agency's cancer studies which are based on five levels of evidence ranging from clear evidence to no evidence, and inadequate study.
- Recipients of the Outstanding New Environmental Scientists (ONES) awards presented their work at a meeting Dec. 11, 2008, in Rodbell Auditorium. The awards recognize and seek to advance the careers of outstanding junior investigators.
- The National Toxicology Program Board of Scientific Counselors will meet Feb. 24, 2009, to peer review five draft substance profiles for candidate substances under consideration for listing in the 12th Report on Carcinogens.
- Off-campus satellite office space for NIEHS has been consolidated from two buildings in locations further from the main campus to one, three-story structure, the Keystone Building, about a mile away. This improves the access of these staff members to each other and makes their commute to the main campus shorter. The move was accomplished between late November and mid January.
- Samuel Wilson, M.D., who has served as Acting Director for NIEHS and NTP over past months, has elected to return to laboratory work fulltime, in the DNA Repair and Nucleic Acid Enzymology group within the Laboratory of Structural Biology of our Division of Intramural Research. His work on behalf of the Institute in a very challenging time is deeply appreciated by the new Director and the entire Institute staff.

Legislative Report

FY 2009 Appropriations

A chart showing the FY 2009 appropriations numbers is shown on the following page.

During December Senate and House members and staff negotiated the marks for the nine appropriations bills that have not been passed by the Congress. When those numbers are released, they will be considered by the House and Senate as though they were Conference Committee marks. Indications are that the Labor, HHS Subcommittee mark for NIH is between the House and Senate marks—a plus for NIEHS.

National Institute of Environmental Health Sciences
11 July 2008
FY 2009 Marks

	FY 2007 Comparable	FY 2008 CAA Mark + Supp	FY 2009 President's Request	FY 2009 House Subcommittee	FY 2009 Senate Subcommittee
NIEHS[1]	$ 642,002,000	$ 645,669,000	$ 642,875,000	$ 664,980,000	$ 660,767,000
NIH[1]	$ 28,899,887,000	$ 29,379,524,000[2]	$ 29,229,524,000[7]	$30,379,524,000	$ 30,254,524,000
Common Fund[1]	$ 483,000,000	$ 498,244,000	$ 533,877,000	$ 544,146,000	$ 568,119,000
Superfund[3]	$ 79,117,000	$ 77,546,000	$ 77,546,000	$ 78,074,000[5]	
DOE Training[4]	$ 9,819,369	$ 9,909,000		$ 10,000,000	

[1]Funding authorized by the Public Health Service Act and falls under the jurisdiction of the Labor, HHS, ED and related Agencies Appropriations Subcommittees. The FY 2008 marks include $3,416,000 for NIEHS, $150,000,000 for NIH, and $2,636,000 for the Common Fund from the first FY 2008 supplemental to be used for scientific research.

[2]This amount includes $295,000,000 for the Global AIDS Fund transfer and $983,000 for the HHS Autism Transfer.

[3]Funding authorized by the Superfund Amendments and Reauthorization Act of 1986 and falls under the jurisdiction of the Interior, Environment and Related Agencies Appropriations Subcommittees. Neither the House nor the Senate Report designates the amount of funding for the NIEHS Superfund Research or Worker Training Programs. In the FY 2009 Congressional Justification sent to the Congress by OMB, the FY 2008 CAA Mark and FY 2009 President's Request for research are $ 49,629,000 and for worker training $27,917,000.

[4]The Department of Energy (DOE) is required by Congressional mandate to provide training to people who cleanup DOE sites. Rather than establish its own program, DOE transfers the funding to NIEHS to manage the DOE Worker Training Program. The Energy and Water Appropriations Subcommittees have jurisdiction.

[5]The House Subcommittee earmarked the $528,000 increase for the NIEHS Superfund Worker Training Program. I have not seen any documents confirming this number.

[6]I have not seen any documents confirming this number.

[7]This amount includes $300,000,000 for Global AIDS.

FY 2009 Stimulus

The House Appropriations Committee released a summary of their stimulus bill. It provides $2 billion for NIH, including $1.5 billion for expanding good jobs in biomedical research to study diseases such as Alzheimer's, Parkinson's, cancer and heart disease, and $500 million to implement the repair and improvement strategic plan developed by the NIH for its campuses. The bill has been passed by the House and has been under consideration by the Senate as of this writing.

FY 2010 Appropriations

The President's Request for FY 2010 is expected to go to the Hill in April.

Breast Cancer – S. 579 and H.R. 1157

In September, the House Energy and Commerce Committee marked up and reported H.R. 1157. The amended bill was passed by the Congress in September and signed by the President on 8 Oct 2008. (P.L. 110-354)

The new law establishes the Interagency Breast Cancer and Environmental Research Coordinating Committee (Committee) to coordinate information on existing activities related to breast cancer and environmental research and make recommendations to the National Institutes of Health and other Federal Agencies on how to improve existing research programs. While the focus of the Coordinating Committee is breast cancer and environmental research, this focus should not be interpreted in a way that would preclude the Committee from taking into account the important role of basic and other cancer research in advancing understanding of the etiology of breast cancer.

The Committee shall (1) share and coordinate information on existing research activities and make recommendations to the National Institutes of Health (NIH) and other Federal agencies by identifying research gaps and scientific opportunities to improve existing research programs related to the environmental causes of breast cancer; (2) develop a comprehensive strategy and advise the NIH and other Federal agencies in the solicitation of proposals for collaborative, multidisciplinary research, including proposals to evaluate environmental and genomic factors that may be related to the etiology of breast cancer; (3) develop a summary of advances in breast cancer research supported or conducted by Federal agencies relevant to the diagnosis, prevention, and treatment of cancer and other diseases and disorders; and (4) make recommendations to the Secretary regarding any appropriate changes to research activities, to ensure that federal research activities are free of duplication of effort, how to increase the involvement of patient advocacy and community organizations, how to best disseminate information on breast cancer research progress, and how to expand partnerships between public and private entities to expand collaborative, cross-cutting research.

Membership includes seven federal officials (CDC, NIH, DoD, and others as deemed appropriate), six members who are scientists, physicians, or other health professionals, and six members of the public who represent people with breast cancer.

In addition, P.L. 110-354 authorizes $40 million to carry out research to evaluate environmental and genomic factors that may be related to the etiology of breast cancer. (This is an authorization only and does not mean that the funds have been appropriated.) Research on other forms of cancer may be included when doing so may advance research in breast cancer or advance research in other forms of cancer.

NIH/Building 1 Information and Updates

NIH Governance

Biennial Report of the Director

NIH released the first Biennial Report of the Director in January 2009 and it provides an integrated portrait of NIH research activities. The report makes it easier for Congress, advocates and patient groups, and the general public to understand the many programs within the agency.

The report contains an assessment of the state of biomedical and behavioral research organized by disease category, investigative approach, or resource. To ensure that the document reflects the work of all 27 Institutes and Centers (ICs), 15 trans-NIH teams gathered, reviewed, and organized information into a standardized format. The report is available at http://report.nih.gov/biennialreport/

Peer Review

In March 2008, NIH released the final report on the new peer review process, which identified the most significant challenges and proposed recommendations that would enhance the peer review system. The areas of implementation are organized into the following four priority areas: 1) Engage the best reviewers; 2) Improve the quality and transparency of review; 3) ensure balanced and fair reviews across scientific fields and reduce administrative burden; and 4) continuous evaluation of peer review. The NIH will begin implementing changes in the Fiscal Year 2010 funding cycle. Investigators submitting applications in January 2009 and later should be aware of the following new policies. Changes to the peer review process for both reviewers and applicants can be found at: http://enhancing-peer-review.nih.gov/

New Investigator Policies

New Investigator policies, stemming from the NIH Enhancing Peer Review Initiative have been revised along with a new policy announcement. Under this new policy, the NIH intends to support New Investigators at success rates comparable to those for established investigators submitting new applications. Early Stage Investigators (ESIs), should comprise a majority of the New Investigators supported. In addition, New Investigator applications will be clustered during review whenever possible. http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-013.html

Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)

The Division of Program Coordination, Planning, and Strategic Initiatives (pronounced Dee-Poughkeepsie) has now been established as mandated in the 2006 NIH Reform Act. It encompasses the former OPASI (the Office of Program Analysis and Strategic Initiatives) as well as the Offices of AIDS Research, Disease Prevention, Behavioral and Social Sciences Research,

and the Office of Research on Women's Health. DPCPSI has lead roles for the NIH Roadmap, the NIH Council of Councils, and the Research, Condition and Disease Categorization project, and for facilitating and reporting on trans-NIH collaborations.

Research, Condition and Disease Categorization (RCDC)
In January 2009, the National Institutes of Health (NIH) launched the public Research, Condition, and Disease Categorization (RCDC) website: http://report.nih.gov/rcdc/ RCDC begins a new process for providing detailed funding information for 215 major areas using knowledge management and computerized, standardized tools. The RCDC process was initiated at the request of Congress to provide consistent and transparent NIH research funding information. For the first time, project listings and the associated dollar amounts are available to the public. By clicking on each of the categories, the user can access full project listings for that category and view, print, or download the detailed report. The RCDC webpage is part of the RePORT website (see paragraph about RePORT below).

Transformative R01 Program
The NIH announced a new Roadmap program, titled the Transformative R01 Program (T-R01s), designed to attract the development of highly creative, paradigm-busting, "out-of-the-box" projects. Special areas of Highlighted Need have been identified for the program. The NIH recognizes that new paradigms are needed in these areas and will strongly encourage research that addresses these needs. The broad topics highlighted in this endeavor include:

- Understanding and Facilitating Human Behavior Change
- Complex 3-D Tissue Models
- Functional Variation in Mitochondria in Human Disease
- Transition from Acute to Chronic Pain
- Formulation of Novel Protein Capture Reagents
- Providing an Evidence Base for Pharmacogenomics

Pioneer Award Program
The NIH Director's Pioneer Award Program is a unique aspect of the NIH Roadmap for Medical Research, a high-risk research initiative of Research Teams of the Future. Pioneer Awards are designed to support individual scientists of exceptional creativity who propose pioneering – and possibly transforming approaches - to major challenges in biomedical and behavioral research. The recent award recipients, the 2009 request for applications and program announcement can all be found at this website: http://nihroadmap.nih.gov/pioneer/index.aspx

Office of Extramural Research (OER)

NIH Offers New Research Portfolio On-Line Reporting Tool (RePORT)
The NIH Office of Extramural Research (OER) has posted its new website and on-line reporting tool, RePORT. This is valuable tool for those searching for data and analyses of NIH research programs and activities, as well as links to CRISP, a glossary of reporting terminology, FAQs, and more. RePORT also provides a detailed listing of funding information, called Research, Condition, and Disease Categorization (RCDC), as mentioned above in the DPCPSI section. More about the RePORT website can be found at http://report.nih.gov/

Adobe Application Forms

Transition to Adobe officially began on December 5, 2008, when NIH updated more than 500 active Funding Opportunity Announcements (FOAs) with Adobe-based application packages and closed their PureEdge predecessors. The new Adobe forms are required for submission for most receipt dates in January and beyond. This transition means submissions will be electronic and integrated with Grant.gov's centralized website.

Maintaining Objectivity in Research – Conflict of Interest Information

The NIH, in collaboration with grantee institutions and with its employees, works to maintain the highest standard of objectivity in all its research endeavors. Correspondingly, various measures have been instituted to address extramural Financial Conflicts of Interest (FCOI) issues quickly and carefully. An expanded FAQ document has been posted about the relevant regulations on the OER website - http://grants.nih.gov/grants/policy/coifaq.htm - and a Web-based Tutorial will soon published, which will thoroughly review the roles and responsibilities of the NIH, awardee Institutions, and Investigators. Also, a Web-based reporting and tracking tool that provides a central place for collection of all FCOI reports received across the NIH will improve monitoring of FCOI reports.

Medical Research with Animals: For Researchers and Institutions

A NIH website has been developed to support NIH-funded scientists using animal models. The url for this website is: http://grants.nih.gov/grants/policy/air/researchers_institutions.htm The new website is a resource for researchers, and institutions that use animals in NIH-supported science; it provides guidance for preparedness and crisis management by researchers and institutions; and it also provides quick access to funding opportunities focused on animals in research, resources to assist with grant writing, and training and education for animal care and use, models, and science and ethics. A sister site designed for the general public is set to be launched in the near future.

Other Items of Interest

Science of Eliminating Health Disparities

December 2008 - The NIH Summit: The Science of Eliminating Health Disparities explored how the integration of Science, Practice, and Policy furthered this research agenda. More than 4000 scientists, practitioners, and community members showcased the collective contribution of the NIH in the development of new knowledge in the science of eliminating health disparities. http://nexus.od.nih.gov/nexus/nexus.aspx?ID=185&Month=12&Year=2008

NIH Research Radio and Podcasts

NIH Research Radio features in-depth interviews with NIH scientists and grantees discussing the latest research findings, educational campaigns, consumer-orientated features, and results from Consensus and State of the Science conferences. Each program runs approximately 30 minutes. NIH Research Radio, which is currently ranked among iTunes Top 100 Medicine Podcasts, is updated every other Friday. Go to http://www.nih.gov/news/radio/nihpodcast.htm to subscribe to the RSS news feed or listen to podcast via your computer. For more information, contact Joseph Balintfy at 301-496-7246.

NIEHS Office of Communications and Public Liaison (OCPL)
September 2008–February 2009

I. NEWS EVENTS

Announcing the Selection of the new NIEHS/NTP Director

On December 3, 2008, the NIH issued a press release announcing a new director for NIEHS. The press release entitled "Linda S. Birnbaum, Ph.D., D.A.B.T., A.T.S., Named New Director of the National Institute of Environmental Health Sciences" was circulated by OPCL to the media, NIEHS staff, grantees, Council and other distribution lists. The announcement with a photo and a bio was added to the NIEHS website. OCPL coordinated several interviews including stories in **Science, The Scientist**, **Science News**, **Occupational Health and Safety**, **The News and Observer**, **Chemical and Engineering News, Effect Measure**, **Inside EPA,** the **NIH Record** and others.

On February 2, 2009, **Chemical and Engineering News** ran a two-page feature article on Linda Birnbaum. The article entitled "New Leader Takes Over at NIEHS: Toxicologist Linda Birnbaum charts course for NIH institute" includes photos, audio clips about Birnbaum's research, and an extensive interview.

Disseminating the Release of Final NTP Report on Bisphenol A — September 3, 2008

OCPL and NTP staff worked together to develop a wide variety of materials to announce and explain the conclusions in the "NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects on Bisphenol A." OCPL updated the NIEHS and NTP web pages related to BPA, including adding a new "Bisphenol A Update" photo and icon on the front of the NIEHS and NTP home pages, adding audio clips and transcripts from the NTP spokespersons, developing a new fact sheet on BPA, and updating its "Since You Asked" pages for the media and public.

On September 3, 2008, OCPL issued a press release entitled "NTP Finalizes Report on Bisphenol A." Approximately 400 stories were reported in various media outlets including **Bloomberg News, Chemical and Engineering News, CNN Money, Environment News Service, Web MD, Associated Press, Washington Post, New York Times, Time magazine** and many others.

In October, November and December 2008, numerous stories following the FDA's risk assessment decision regarding BPA mentioned the NTP findings. Several stories including one in **Time** magazine on November 2, 2008, and a November 1, 2008 editorial in the **New York Times,** included quotes from NTP Associate Director John Bucher. On December 30, 2008, **USA Today** ran a column entitled "Top health stories of '08: Stress, drugs and chemical lows" that mentions the September release of the NTP BPA report.

II. NEWS COVERAGE

Newspapers, Trade Papers and National Magazines

The September 2008 issue of **Glamour** magazine featured a lengthy article entitled "The Scariest Health Threat You've Never Heard Of" that included quotes from DIR physician/ scientist Fred Miller.

In September 2008, several stories focused on the NIEHS-led Sister Study, including a piece by an **ABC affiliate** in Miss. and one in **Medical News Today** entitled "Sisters of Good Morning America's Robin Roberts Join Sister Study for Breast Cancer Research."

On September 12, 2008, **Cell-Based Assay News** developed a story called "NTP Hosts RFI Meeting to Develop 'Rigorous, Comprehensive' HTS Toxicity-Screen Battery."

On September 16, 2008, OCPL worked with DERT staff to issue a press release entitled, "NIEHS Invests $21.25 Million to Find Environmental Causes of Parkinson's Disease." A story in **Health News** entitled "Deep Pockets Being Opened for Parkinson's Research" highlighted the new funding. A few months later, on December 9, 2008, a related story appeared in the **Chronicle of Higher Education** entitled "Hidden Hazards: Could pollutants trigger Alzheimer's and Parkinson's diseases?" that featured NIEHS-supported research on the topic and quotes by Freya Kamel of DIR.

On September 23, 2008, the **University of Arizona** highlighted several of the key speakers that participated in the NIEHS Hispanic Heritage event held at NIEHS. The event highlighted NIEHS' commitment to educational outreach to the Hispanic community.

On September 29, 2008, **The New York Sun** announced that former NIEHS Director Ken Olden would be the founding dean of the CUNY School of Public Health at Hunter College.

On September 29, 2008, NIEHS teamed with other NIH institutes to issue an announcement about a new NIH Roadmap program. The release entitled **"**NIH Announces Funding for New Epigenomics Initiative" highlights that the NIH will invest more than $190 million over the next five years to accelerate epigenomics research, an emerging field of biomedical research. Several media outlets spread the word, including a story in **Curetoday.com** in December that included quotes from Fred Tyson of DERT.

The October 2008 issue of **Self Magazine** included an interview with Retha Newbold of DIR for several stories in this issue, including "Cancer in a Can?" and "Steering Clear of BPA."

On October 5 and 6, 2008, **The Times-Tribune** ran a two-part series on power lines. NIEHS Associate Director Chris Portier is quoted.

On October 6, 2008, **The Toledo Blade** published a story entitled "Sister study focuses on genetic link to cancer" which focuses on the NIEHS-led prospective study. Lisa DeRoo of DIR is quoted.

On October 7, 2008, the local N.C. paper, **The News and Observer,** ran a story entitled "Telecommuters look smart as gas prices go up" that focuses on teleworking efforts in Research Triangle Park. Dick Sloane of the Office of Management (OM) and Gloria Jahnke of the NTP were quoted about NIEHS efforts.

The October 20, 2008 issue of **People** magazine included a major story about the NIEHS-sponsored Sister Study including a quote by Dale Sandler of DIR.

On October 21, 2008, **The New York Times** ran a story entitled "Dentists Back Sealants, Despite Concerns" that focused on the chemical BPA. The story mentioned the NTP findings.

On October 29, 2008, the **University of Kentucky** issued a press release announcing that NIEHS Acting Deputy Director Bill Suk and NIEHS grantee Phil Landrigan joined with three doctoral students to launch a new environmental series at the University.

The November 2008 issue of **Nature Medicine** included a story entitled "As IVF becomes more common, some concerns remain" that includes quotes from Carmen Williams of DIR.

On November 12, 2008, a story published online in **Environmental Health News** entitled "Enviro health scientists, chemists join forces to promote safe chemicals" includes quotes from Jerry Heindel of DERT.

On November 12, 2008, local N.C. paper, **The News and Observer**, included a story entitled "Looking at drugs in water" that included quotes from former NIEHS Director Ken Olden.

On November 16, 2008, local N.C. paper, **The News and Observer,** ran a story about BPA entitled "Some moms ditch plastic cups" that includes the findings of the NTP report.

On November 19, 2008, OCPL worked with NTP and NICHD staff to issue a joint NIEHS/NICHD press release entitled "ADHD Medications Do Not Cause Genetic Damage in Children." The release resulted in stories in the **Washington Post, Reuters, Web MD, UPI,** and **Consumer Affairs.com**.

On December 2, 2008, **Reuters Health** featured a story entitled "Fibroid growth differs in black and white women" about a new DIR-supported paper in PNAS. Donna Baird of DIR was quoted.

On December 16, 2008, **The New York Times** responded to a public inquiry related to electromagnetic devices. Associate Director Chris Portier was quoted.

On December 18, 2008, the National Research Council (NRC) issued a report to EPA on phthalates. Paul Foster of NTP was on the NRC panel and was quoted in numerous media outlets including **Science News and USA Today**.

On December 26, 2008, **Reuters** ran a story entitled "Pain pills may cut risk of bowel cancer: study" that includes quotes from Sangmi Kim of DIR.

On December 26, 2008, the **Washington Post** ran a story related to climate change and pollutants that included a quote from EHP editor Hugh Tilson.

Beginning January 5, 2009, an XM satellite radio program geared toward medical providers called **Reach MD** ran a 15 minute interview with Retha Newbold of DIR entitled "Concerns Over Bisphenol A (BPA) Exposure." To listen to the program or view a copy of the transcript, go to http://www.reachmd.com/xmsegment.aspx?sid=3976.

On January 8, 2008, **The Huffington Post** highlighted the NIEHS-funded work at the University of California, Davis that focuses on autism.

The January 13, 2009 issue of the **Daily Environment Report** included quotes from NTP Associate Director John Bucher for the annual "2009 Outlook" article.

The January 22, 2009 issue of **Discover Magazine** included a story entitled "Is One Very Tough Rat a Very Big Risk to Human Health?" The story includes quotes from Jef French of NTP.

On January 23, 2009, **Congressional Quarterly Press** published a 20+ page report entitled "Regulating Toxic Chemicals" that included quotes from NTP Associate Director John Bucher.

On January 25, 2009, the **Washington Post** ran a story entitled "Database Helps Assess Your Breast Cancer Risk" that references the NIEHS.

On February 1, 2009, the **Journal of the American Veterinary Medical Association (JAVMA)** ran an article entitled "Training program brings veterinary pathologists to NIH" that includes information about Mark Hoenerhoff of DIR.

On February 3, 2009, OCPL worked with DIR staff and Duke University to issue a press release entitled "Research Finds New Cause of Ozone Wheezing and Potential Treatments." A story in the **Arizona Republic** included quotes from Stavros Garantziotis of DIR.

III. PUBLIC INFORMATION AND OUTREACH MATERIALS

Media Training. On September 29 and 30, 2008, OCPL teamed with trainers from The Communication Center in Washington to provide tailored, small-group training to 15 scientists in the Institute, to help them more effectively communicate their science findings to the media. http://www.niehs.nih.gov/news/newsletter/2008/november/working-with.cfm

Presentations Skills Training. In January 2009, OCPL teamed with the National Toxicology Program (NTP) to sponsor two training sessions for about 24 NIEHS scientists and administrators in January. The two-day sessions were specifically designed to help NIEHS staff improve their presentation skills. Scientists from the Divisions of Intramural Research (DIR), Extramural Research and Training (DERT), as well as the NTP, participated. Each participant gave a ten minute presentation that was critiqued by the trainer and other attendees. The training was led by Rick Grandinetti of VisionPlanning, Inc. in Morrisville, N.C. http://www.niehs.nih.gov/news/newsletter/2009/february/scientists-get-tips.cfm

Chinese DelegationVisit. On November 14, 2008, OCPL staff worked with Deputy Scientific Director Bill Schrader of DIR to host a contingent of Chinese government officials involved in a four-month executive education and English-language immersion program at Duke University. The delegation attended a half-day workshop at NIEHS as part of their series of weekly field experiences. NIEHS division heads presented overviews of the scientific activities and organizational structure of their respective areas during the visit. The NIEHS visit also featured Chinese-born scientists working at NIEHS, who presented talks in their native Mandarin Chinese. http://www.niehs.nih.gov/news/newsletter/2008/december/chinese-delegation.cfm

Environmental Journalists. In mid-October 2008, the OCPL Director and News Director participated in the 18th Annual Conference of the Society of Environmental Journalists in Roanoke, Va., that was attended by more than 800 reporters. The OCPL staffers met with many of the reporters, disseminated information, and supported the efforts of Gwen Collman and Jerry Heindel of DERT as they participated in several events.

Online Newsletter. OCPL continued to increase readership of the NIEHS monthly online newsletter called the **Environmental Factor** that highlights NIEHS research, staff accomplishments and ongoing activities.
http://www.niehs.nih.gov/news/newsletter/index.cfm

National Conferences. OCPL worked with others in the Institute to sponsor the consolidated exhibit at the American Public Health Association (APHA) Annual Meeting in San Diego, October 25–29, 2008. OCPL supported the efforts of NIEHS scientists and administrators presenting at APHA. OCPL also joined with others in the Institute to staff the NIEHS consolidated exhibit at the American Association for Advancement of Science (AAAS) in Chicago in mid-February 2008.

Intranet Redesign. OCPL staff hosted 45 group and individual meetings throughout the NIEHS as part of the Intranet (Junction) needs assessment. This assessment is funded by competitive set-aside funds from the NIH Office of the Director (OD).

Total New Coverage for NIEHS Science, Researchers and Activities
In September 2008, NIEHS was cited in 633 news stories.
In October 2008, NIEHS was cited in 532 news stories.
In November 2008, NIEHS was cited in 367 news stories.
In December 2008, NIEHS was cited in 189 news stories
In January 2009, NIEHS was cited in 266 news stories.

Christine Bruske Flowers
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NIEHS
Office of Communications
and
Public Liaison (OCPL)

September 2008 – February 2009

Council Report Attachments

12 December 2008:
Vol. 322. no. 5908, p. 1617

NEW BOSS AT NIEHS

Linda Birnbaum, a longtime government toxicologist, has been named director of the $730 million National Institute of Environmental Health Sciences (NIEHS) in Research Triangle Park, North Carolina. Birnbaum succeeds David Schwartz, who left in February amid ethics concerns (*Science*, 22 February, p. 1021).

Birnbaum, who takes over next month, is an expert on the health effects of dioxin and other hormonelike pollutants. She has spent nearly 29 years in government, first at NIEHS and more recently at the Environmental Protection Agency's research lab near NIEHS. Some researchers are worried that Birnbaum might be less supportive of investigator-initiated research than of studies to support regulations. On the other hand, her research has bridged both because "it's been very focused on [biological] mechanisms," says toxicologist David Eaton of the University of Washington, Seattle, who says Birnbaum "is well-prepared to lead NIEHS." Birnbaum says any concerns about a decline in blue-sky basic research are "unfounded" and adds that "it's still going to be extremely important."

Birnbaum sees "a lot of opportunities for improvement" at the institute. For example, she wants to look more closely at whether the trace levels of pollutants in most Americans are harmful.

http://www.sciencemag.org/cgi/reprint/322/5908/1617c.pdf

TheScientist.com
MAGAZINE OF THE LIFE SCIENCES

NIEHS gets new leader

News Blog
Posted by Bob Grant
[Entry posted at 3rd December 2008 05:32 PM GMT]

Linda Birnbaum, a toxicologist and former head of EPA's Experimental Toxicology Division, will be the new head of the NIH's National Institute of Environmental Health Sciences (NIEHS), ending a period of turmoil under her predecessor David Schwartz, who resigned from the institute early this year amidst allegations of mismanagement.

Raynard Kington, acting head of NIH, announced the appointment today (Dec. 3).

"I look forward to Dr. Birnbaum joining us," Kington said in a statement. "She has a long and distinguished career conducting research into the health effects of environmental pollutants, and the cause and effects relationships at pollutant concentrations which mimic those occurring in the environment."

"I am excited about serving as the director of NIEHS at a time when integration across disciplines is essential, from molecular biology to pharmacology and physiology to epidemiology. Complex environmental issues require individual and team efforts to address the interactions between the environment and human health," Birnbaum said in a statement.

Birnbaum will assume leadership of NIEHS starting in January, 2009.

http://www.the-scientist.com/blog/display/55257/

TheScientist.com
MAGAZINE OF THE LIFE SCIENCES

New NIEHS leader looks ahead

NewsBlog
Posted by Bob Grant
9th December 2008 04:00 PM GMT]

Researchers at NIH's long-beleaguered National Institute of Environmental Health Sciences (NIEHS) are hopeful that the institute's new head, toxicologist Linda Birnbaum will be able to right the ship after the rocky tenure of ex-NIEHS director David Schwartz.

Chris Portier, associate director of NIEHS, said that there are key differences between Schwartz and Birnbaum. "I'm much more optimistic that she's got management experience of a large group, which David [Schwartz} didn't have," he told The Scientist. "She's got governmental experience, which David didn't have. It will be a completely different person that steps into that office."

Amid allegations of mismanagement -- including stocking his disproportionately large lab full of former Duke University colleagues -- Schwartz resigned from his post earlier this year. One of his most provocative moves was to suggest privatizing and cutting funding for Environmental Health Perspectives, NIEHS's open-access, peer-reviewed journal. The proposition raised hackles in Washington, DC and beyond, among members of the environmental health and science community.

When asked about how she plans on correcting any damage that former NIEHS director David Schwartz may have done to the institute, Birnbaum demurred. "I don't focus on the past," she said. "I'm looking ahead."

Birnbaum did say that she is in favor of keeping EHP publically funded. "I've always been a strong supporter of EHP," she told The Scientist. "I feel very fortunate to have it as part of the NIEHS portfolio."

Birnbaum, who formerly headed the EPA's Experimental Toxicology Division, will be taking over as the director of NIEHS in January. She said she will encourage increased interaction between basic and applied scientists, from bench researchers to epidemiologists and physicians, at the institute.

"I'm someone who believes in the synergy that can come from different kinds of science," she said.

Birnbaum also said she will focus on both the prevention and treatment of environmentally-mediated diseases and that she'll direct more attention to cutting edge technologies, such as biomarkers to track the early effects of asbestos exposure. "These are things that haven't been addressed a lot that offer us real opportunities," she said.

Portier, who also studies systems biology at NIEHS, agreed that an integrative approach was essential to the success of the institute. "I agree 100% that we're going to have to do much better integrative science if we're going to address the challenges we're facing now," he said. "[Birnbaum's] really quite a perfect choice for the institute."

http://www.the-scientist.com/blog/display/55271/

ScienceNews

Toxicologist to Become an NIH Director

By Janet Raloff
Web edition: Wednesday, December 3rd, 2008

Long-time readers of *Science News* will recognize the name Linda Birnbaum. Today, this toxicologist — an expert not only on dioxins and their kin, but also on brominated flame retardants— was named the incoming director of the National Institute of Environmental Health Sciences. It's one of the smaller siblings among 27 members of the NIH family and the only one devoted to understanding environmental causes of disease.

The institute Birnbaum takes over on Jan. 1 is located in Research Triangle Park, N.C. Well removed from NIH's main campus here in the DC burbs, it's been where Birnbaum has spent most of her working career — first at NIEHS, and later at the Environmental Protection Agency. Indeed, for 16 years she served as EPA's director of experimental toxicology.

NIEHS is probably best known as the publisher of *Environmental Health Perspectives*, an open-access peer-reviewed journal on environmental risks and hazards. But with a $730 million budget, NIEHS also funds 1,240 scientific grants. Internal research at the agency has, over the decades, made many of the discoveries that underlie a burgeoning field of science that has come to be known as endocrine disruption — or hormone mimicry by environmental agents.

Active in research, Birnbaum has been an author on more than 600 peer-reviewed journal articles, book chapters, abstracts, and reports. She's president-elect of the International Union of Toxicology(an umbrella group of societies in more than 50 countries), a recent president of the Society of Toxicology(the world's largest professional organization of toxicologists), and former chair of toxicology at the American Society of Pharmacology and Therapeutics. In other words, she has the creds.

I'm more familiar with another side of her professional persona: the communicator.

As a reporter who has worked with Birnbaum for probably 20 years, I've found her singularly articulate in explaining the often arcane effects and mechanisms by which many environmental agents cause harm. A straight shooter, she won't hazard wild guesses about implications of her data, but she will offer informed speculation. The kind of comments, for instance, she'd share with colleagues at a research conference.

She doesn't look for attention or grandstand, but she will speak up repeatedly to keep colleagues grounded on what the data that they're considering show — or don't show. She also points out what kinds of studies would be required to fill in all those niggling data gaps. These would be the investigations needed to understand whether the chemicals we encounter in the home, workplace and environment are likely to be benign or not — at the doses to which we may be exposed.

Earlier this year, David Schwartz resigned from his post as NIEHS director under a very gray cloud. One of his sins: He tried to undertake a quick privatizatiop of *Environmental Health Perspectives*. Researchers and many Capitol Hill investigators suspected this would effectively kill the publication or keep it from publishing groundbreaking data on issues the Bush administration would prefer not come to light. EHP remains a wholly owned government-administered entity. But the likelihood it would be sold or materially changed remained touch-and-go for a long time.

Schwartz also had a distinctly different attitude than Birnbaum about the news media. He encouraged his staff to shun reporters or to find ways to limit contact with them as much as possible. Schwartz also had been under congressional scrutiny for alleged ethics violations.

As people look for science to once again hold sway in research agencies, appointments like Birnbaum's appear to be a step in the right direction.

http://www.sciencenews.org/view/generic/id/39012/title/Toxicologist_to_Become_an_NIH_Director

New Director Named for NIEHS

December 05, 2008

The next director of the National Institute of Environmental Health Sciences (NIEHS) will be Linda S. Birnbaum, Ph.D., who is currently a senior adviser with EPA but previously worked at NIEHS for a decade. Dr. Raynard S. Kington, acting director of the National Institutes of Health, announced her appointment Wednesday. Birnbaum will start in January; she previously spent 16 years as director of EPA's Experimental Toxicology Division and was president of the Society of Toxicology in 2004-05.

NIEHS has a $730 million budget to fund biomedical research programs, prevention, and intervention efforts. It is located in Research Triangle Park, N.C., and currently is funding more than 1,240 research grants, according to the NIH announcement. "I am excited about serving as the director of NIEHS at a time when integration across disciplines is essential, from molecular biology to pharmacology and physiology to epidemiology. Complex environmental issues require individual and team efforts to address the interactions between the environment and human health," Birnbaum said in that announcement. "Chronic exposures and chronic diseases can have multiple causative factors. A broad array of scientific expertise is needed to understand such problems in order to prevent disease. I am eager to translate the work of the basic scientist and epidemiologist into improvements for the health of our citizens and communities."

Birnbaum is the author of more than 600 peer-reviewed publications who has received numerous awards during her career, including the Women in Toxicology Elsevier Mentoring Award, the Society of Toxicology Public Communications Award, EPA's Health Science Achievement Award and Diversity Leadership Award, and 12 Science and Technology Achievement Awards.

http://ohsonline.com/articles/2008/12/5-new-director-named-for-niehs.aspx

THE NEWS&OBSERVER
newsobserver.com

Published: Dec 04, 2008 12:30 AM
Modified: Dec 04, 2008 02:45 AM

EPA scientist returns to NIEHS as its director

By Wade Rawlins, Staff Writer

Dr. Linda Birnbaum, a federal scientist who has been a senior adviser at the U.S. Environmental Protection Agency, was appointed Wednesday as director of the National Institute of Environmental Health Sciences, which is in Research Triangle Park.

Birnbaum, 61, succeeds David Schwartz, whose leadership of the agency drew congressional scrutiny over spending and alleged conflicts of interest. Schwartz left in April to take a post as a researcher at the National Jewish Medical and Research Center in Denver, Colo. Birnbaum's appointment was announced by Raynard Kington, acting director of the National Institutes of Health.

NIEHS is a branch of the National Institutes of Health. It has a $730 million budget and supports research to understand the effects of the environment on human health. About 1,500 federal employees, research fellows, contractors, students and guest researchers work there.

"NIEHS is really the premier organization conducting environmental health research in the world," Birnbaum said in an interview. "I want to ensure we continue to be that organization."

Asked about her predecessor's rocky tenure, Birnbaum said, "I think there were some legitimate concerns. David had a very exciting vision that he was eager to implement. I don't think he was used to working in the government."

After coming under fire for testifying in plaintiffs' lawsuits after he became director and for filing expense reports for items some questioned as excessive, Schwartz stepped aside from his official duties of the NIEHS director in August 2007. Samuel Wilson stepped in as acting director, and Schwartz became a senior advisor for environmental health sciences to the NIH director.

Unlike Schwartz, a pulmonologist who came to NIEHS from Duke University, Birnbaum has worked as a government scientist for nearly 30 years in the Triangle. She and her husband, David Birnbaum, a retired mathematician, live in Chapel Hill.

A native of New Jersey, Birnbaum trained as a microbiologist at the University of Illinois, Urbana, where she earned a doctorate. After a stint teaching in New York and working at a private research lab studying the causes of aging, she moved to North Carolina in 1979 and began work as a senior staff fellow at NIEHS. Her research focused on how environmental pollutants such as dioxins and polychlorinated biphenyls get into humans and how the body handles them.

"My love has been these very persistent chemicals," Birnbaum said.

She moved up the ranks, eventually becoming director of the institute's chemical disposition group. She left NIEHS after 10 years to work at the EPA.

Birnbaum will begin in January.

http://www.newsobserver.com/news/story/1319926.html

CHEMICAL & ENGINEERING NEWS

December 8, 2008
Volume 86, Number 49
p. 26

Birnbaum Picked To Head NIEHS

By David J. Hanson

Cheryl Hogue/C&EN
Birnbaum

Linda S. Birnbaum has been appointed the new director of the National Institute of Environmental Health Sciences and the National Toxicology Program. Birnbaum is a widely respected toxicologist who has studied the impact of environmental chemicals for almost 29 years at NIEHS and EPA. Birnbaum headed EPA's Experimental Toxicology Division for 16 years. At the announcement of her appointment by NIH Acting Director Raynard S. Kington, Birnbaum said she was excited about the job. "Chronic exposures and chronic disease can have multiple causative factors. I am eager to translate the work of the basic scientist and epidemiologist into improvements for the health of our citizens and communities," she said. The appointment will be effective in January 2009.

http://pubs.acs.org/isubscribe/journals/cen/86/i49/html/8649govc3.html

Effect Measure

Key NIH institute gets a new Director

Posted on: December 5, 2008 7:45 AM, by revere

Environmental health researchers got some good news yesterday. The NIH's only institute that focusses almost entirely on public health and environmental science, the National Institute of Environmental Health Sciences (NIEHS), got a new Director after years of chaotic and controversial regime of former Director David Schwartz, who left under a cloud of alleged conflicts of interest and mismanagement. For the last year NIEHS has been under very capable and stabilizing direction of an Acting Director, Sam Wilson, but there were limits on what could be done by a Director and his Deputy who didn't have permanent status. Now the answer as to who will guide this very important NIH institute into the 21st Century, and it is a welcome one. The New Director will be Dr. Linda Birnbaum, a highly respected scientist in her own right with a track record of scientific leadership in the profession and someone who knows the ropes of the government science world, having been a researcher at NIEHS or EPA for the last 30 years.

NIEHS is not geographically with the other NIH institutes in Bethesda, Maryland, but down in North Carolina's Research Triangle Park area cheek by jowl with Raleigh - Durham. It is situated on a lovely artificial lake, across which one can see the EPA's research facility where Birnbaum now works as director of experimental toxicology. In the interests of full disclosure I admit to knowing and being a fan of Dr. Birnbaum's, so consider that when judging my optimism for this appointment. While this is not a Presidential appointment, *per se*, like Obama's cabinet and staff appointments it is characterized by high competence and a pragmatic a straightforward character. I know her primarily through scientific relationships, where she is enormously productive of work of high importance in the field. Her specialty involves dioxins and the biology of the dioxin receptor and more recently flame retardants, a growing concern in environmental health. But scientists are usually enthusiastic about other scientists, some of whom turn out to be great leaders and some who don't. So I'll also provide you with an informed non-scientist's view of the new Director, that of science journalist Janet Raloff.

Raloff is one of the best science reporters around (I've been interviewed by her and one quickly learns to tell the good ones from the not so good ones on the basis of the questions alone). Her stories in *Science News* are always top notch). And here is what she said there about Birnbaum:

As a reporter who has worked with Birnbaum for probably 20 years, I've found her singularly articulate in explaining the often arcane effects and mechanisms by which many environmental agents cause harm. A straight shooter, she won't hazard wild guesses about implications of her data, but she will offer informed speculation. The kind of comments, for instance, she'd share with colleagues at a research conference. She doesn't look for attention or grandstand, but she will speak up repeatedly to keep colleagues grounded on what the data that they're considering show -- or don't show. She also points out what kinds of studies would be required to fill in all those niggling data gaps. These would be the investigations needed to understand whether the chemicals we encounter in the home, workplace and environment are likely to be benign or not -- at the doses to which we may be exposed. [snip]

As people look for science to once again hold sway in research agencies, appointments like Birnbaum's appear to be a step in the right direction. (Janet Raloff, Science News)

A step in the right direction. Indeed.

http://scienceblogs.com/effectmeasure/2008/12/key_nih_institute_gets_a_new_d.php?utm_source=sbhomepage&utm_medium=link&utm_content=channellink

INSIDEEPA.COM
an online news service from the publishers of Inside EPA

RISK POLICY REPORT - 12/9/2008

Senior EPA Toxicologist Moves To Head Key Toxics Research Agencies

Long-time senior EPA toxicologist Linda Birnbaum is leaving the agency to head the National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP), whose toxicological studies EPA often uses in its chemical risk assessments.

Birnbaum's research at EPA has focused on dioxin and endocrine disrupting compounds.

The former EPA scientist will take over the institute and its $730 million budget that funds multidisciplinary biomedical research programs in January, according to an announcement from the National Institutes of Health, which oversees NIEHS.

Birnbaum's appointment will allow NIEHS and EPA to leverage the other agency's research as they have not done effectively before, says a former EPA staffer. NIEHS and EPA have not communicated well in the past, though their work often converges, the source says. One example is NIEHS' "huge program on endocrine disrupting compounds, which no one at EPA knows about."

Birnbaum's appointment provides an opportunity to "bring these two institutions' research together," the source says, adding that NIEHS should be aware of EPA's data gaps.

In the announcement, Birnbaum emphasized the need to integrate across disciplines. "Complex environmental issues require individual and team efforts to address the interactions between the environment and human health," she said. "Chronic exposures and chronic diseases can have multiple causative factors. A broad array of scientific expertise is needed to understand such problems in order to prevent disease.

Another source says the appointment could create heartburn for industry officials because Birnbaum brings additional muscle to an institution whose work can already spell trouble for some chemicals. If NIEHS identifies a chemical as a carcinogen, it "sounds the death knell for the commercial prospects of identified chemicals," the source says. And, the source says, NIEHS publishes Environmental Health Perspectives, a journal that is viewed as "willing to publish anything that can possibly make a chemical look bad."

"I am excited about serving as the director of NIEHS and NTP at a time when integration across disciplines is essential, from molecular biology to pharmacology and physiology to epidemiology," Birnbaum said.

http://insideepa.com/secure/docnum.asp?f=epa_2001.ask&docnum=RISK-15-50-5

NIH Record

NIEHS Welcomes Birnbaum as Next Director

January 9, 2009
By Eddy Ball

NIEHS director Dr. Linda Birnbaum
Photo by: Steve McCaw

Dr. Linda S. Birnbaum will become NIEHS's fifth director in its 43-year history this month. Her appointment was announced in December by NIH acting director Dr. Raynard Kington. Birnbaum has most recently been a senior advisor at the Environmental Protection Agency, where she has served for 16 years as director of the Experimental Toxicology Division.

As director of NIEHS and the National Toxicology Program (NTP), Birnbaum will oversee a $730 million budget that funds multidisciplinary biomedical research programs, prevention and intervention efforts that encompass training, education, technology transfer and community outreach. The institute currently supports more than 1,240 research grants.

"I am excited about serving as the director of NIEHS at a time when integration across disciplines is essential, from molecular biology to pharmacology and physiology to epidemiology," said Birnbaum. "Complex environmental issues require individual and team efforts to address the interactions between the environment and human health."

A native of New Jersey, she earned her M.S. and Ph.D. in microbiology from the University of Illinois, Urbana. She is a board-certified toxicologist and has served as a federal scientist for nearly 29 years—the first 10 of those at NIEHS—first as a senior staff fellow at NTP, then as a principal investigator and research microbiologist and finally as leader of the institute's chemical disposition group.

Birnbaum has received numerous awards, including the Women in Toxicology Elsevier Mentoring Award, the Society of Toxicology Public Communications Award, EPA's Health Science Achievement Award and Diversity Leadership Award and 12 Science and Technology Achievement Awards, which reflect the recommendations of EPA's external science advisory board, for specific publications.

The author of more than 600 peer-reviewed publications, book chapters, abstracts and reports, Birnbaum's research focuses on the pharmacokinetic behavior of environmental chemicals; mechanisms of actions of toxicants, including endocrine disruption; and linking of real-world exposures to effects. She is also an adjunct professor in the School of Public Health, the toxicology curriculum and the department of environmental sciences and engineering at the University of North Carolina, Chapel Hill, as well as in the integrated toxicology program at Duke University.

Birnbaum's appointment has been well received within the scientific community, where she is a highly regarded member. She is currently president-elect of the International Union of Toxicology, the umbrella organization for toxicology societies in more than 50 countries; former president of the Society of Toxicology, the largest professional organization of toxicologists in the world; former chair of the division of toxicology at the American Society of Pharmacology and Therapeutics; and former vice president of the American Aging Association.

http://nihrecord.od.nih.gov/newsletters/2009/01_09_2009/story3.htm

CHEMICAL & ENGINEERING NEWS (C&EN)

February 2, 2009
Volume 87, Number 05, pp. 24-26

New Leader Takes Over At NIEHS

Toxicologist Linda Birnbaum charts course for NIH institute

By Cheryl Hogue

AS THE NEW ADMINISTRATION settles in, agencies across the federal government are undergoing transitions. But for one leadership change that took place two days before President Barack Obama took the oath of office, the timing was coincidental.

Linda S. Birnbaum, the new director of the National Institute of Environmental Health Sciences (NIEHS), officially assumed her post on Jan. 18 and now oversees an institute with a $730 million annual budget. Located in Research Triangle Park, N.C., and part of the National Institutes of Health, NIEHS is home to the National Toxicology Program, which tests chemicals of concern to public health.

Birnbaum, the first toxicologist to head NIEHS, came to the institute from the Environmental Protection Agency. For 16 years, she served as director of EPA's Experimental Toxicology Division. During her last year at EPA, she coordinated efforts across the agency probing the contamination of Libby, Mont., with asbestos from a vermiculite mine.

Raynard S. Kington, acting director of NIH, says Birnbaum "has a long and distinguished career conducting research into the health effects of environmental pollutants." She is an expert in the toxicology of dioxins, brominated flame retardants, and endocrine-disrupting chemicals in general, and she has authored more than 600 peer-reviewed publications, book chapters, abstracts, and reports. She is a former president of the Society of Toxicology.

Birnbaum comes to an institute that was wracked by political turmoil during the tenure of David A. Schwartz, who was NIEHS director from 2005 to 2007. Schwartz was the target of several congressional investigations, including some involving conflict-of-interest allegations about testifying in lawsuits after he took the job at the institute.

In addition, Schwartz slashed the budget for NIEHS's open-access journal, *Environmental Health Perspectives*, by 85% and attempted to privatize it. (In response to this, the American Chemical Society, publisher of C&EN, at one time expressed interest in taking over *Environmental Health Perspectives*.) Schwartz also shifted the institute's funding to emphasize patient care at the expense of NIEHS's traditional focus on preventive programs. The morale of the staff is reported to have fallen significantly during Schwartz's controversial tenure.

DESPITE ALL that has happened in the recent past, Birnbaum sees great opportunity at NIEHS. "The institute has a marvelous scientific portfolio. It has a lot of excellent people working very hard doing a lot of important things," she tells C&EN.

Although she diplomatically skirts the question of whether she will flat-out reverse Schwartz's policies, Birnbaum has several changes in mind as she sets an agenda for NIEHS.

"Some of my first challenges are to restore morale and develop a culture of openness and trust at the institute," she says.

Besides making efforts within NIEHS, Birnbaum has her eye on reaching out beyond the institute. For instance, although she's left EPA, Birnbaum is by no means severing ties with the agency. NIEHS is situated across a small lake from a major EPA laboratory where Birnbaum worked for 16 years. Pedestrians can easily walk between the facilities via a scenic footpath. But Birnbaum is keenly aware that scientists at these two government research facilities have had little interaction, even though the work of both programs is connected to the effects from chemicals in the environment. She's intent on building virtual bridges between the two.

In addition, Birnbaum wants NIEHS to strengthen its relationships with those outside the government, including scientific organizations and citizen groups. "I'm very excited and optimistic about opportunities to interact," she says.

One avenue of interacting with those outside NIEHS is *Environmental Health Perspectives*. In contrast to Schwartz, Birnbaum is a strong supporter of the publication.

"I am thrilled to see that *Environmental Health Perspectives* has the highest impact factor of any environmental journal," Birnbaum says. "It has a very wide readership," especially in the U.S., Europe, and China (there is an edition in Chinese). "It attracts people from the basic sciences to the most applied sciences, people doing basic chemistry to people doing epidemiology and clinical medicine as well," she says.

Meanwhile, Birnbaum also wants to strengthen NIEHS's connections with other parts of NIH. She says, "I need to work hard to reestablish close working relationships with our sister institutes in Bethesda," the Maryland town where NIH headquarters is located.

Although she has yet to oversee her first budget at NIEHS, Birnbaum indicates that the types of research that the institute funds may change. Specifically, she says the institute should return to its traditional focus on preventive programs.

"There's clearly a role for clinical medicine at NIEHS," Birnbaum says. "However, I think when we're talking about environmental health, it's not only 'bench to bedside,' it is also 'bench to public health.' We have a major role to play in the betterment of public health in this country."

ONE CRITICISM that Birnbaum expects to face involves regulatory decisions on chemicals. The decisions, such as those made by EPA and the Food & Drug Administration, rely on studies like those conducted by the National Toxicology Program in which laboratory animals are given high doses of a substance. Critics say these experiments inappropriately include exposures to chemicals that are far higher than what the public experiences.

"They are missing the point," Birnbaum says of these critics. The amount of a chemical given to a laboratory animal isn't what's relevant in these tests, she explains. "It's what's in the body or in the specific tissue at a specific point in time." In animal studies, she says, "if you actually look at the internal dose, frequently, it's not high."

The key, according to Birnbaum, is finding more sophisticated methods to determine how much of a compound is not just getting into the body but how much is getting into the tissue, where it can adversely affect health.

"I'm willing initially, for incremental improvement, to take what's in the blood" as a surrogate measure of tissue load, Birnbaum says. She notes that for some chemicals, such as dioxins, the concentration of the substance in blood may not be the best measure of tissue exposure inside the body. "At high levels of exposure, it isn't just in blood lipids, there's a heck of a lot of it that's bound up in the liver. So you may underestimate the total amount that's in the body, but it's a lot better than saying how much you were exposed to on a daily basis," she says.

Estimates of how much of a chemical gets to nerves, organs, or other tissue inside a person might also be made using other easily accessible bodily fluids, such as urine. But Birnbaum knows that this line of study—whether involving blood, urine, or other fluids—has limitations.

"Not everybody's eager to give you blood," she says. Plus, some chemicals or their metabolites aren't eliminated in urine. And a single metabolite may have more than one source; the body may transform any of several chemicals into the same end product.

Nonetheless, Birnbaum has hope that new tests based on proteomic or metabonomic technologies will allow researchers to easily study accessible bodily fluids for early signs of toxic responses due to exposure to chemicals. She cautions scientists to keep practicality in mind as they invent this sort of assay, known as an "omic" test. She expresses frustration about new techniques for identifying early signs of toxic response in brain, kidney, and liver cells that fail to heed this caution.

"I don't know too many people who are eager to give you a brain biopsy or a kidney biopsy so you can measure what is going on in that tissue specifically," Birnbaum says. "We have to be able to use easily accessible tissue."

In addition, the omic tests are expensive to carry out, she says, expressing hope that researchers will also develop less costly methods to detect early signs of disease.

High-throughput omic tests for initial toxicity screening of chemicals have captured the attention of the federal government in recent years. The National Toxicology Program is involved in this work, as is EPA through the agency's ToxCast program. While endorsing these new technologies, Birnbaum notes their limitation.

These screening efforts may link some chemicals with health hazards they weren't previously associated with, Birnbaum says. But she worries that results of high-throughput testing may incorrectly indicate that some compounds aren't hazardous when in fact they are.

"I am always concerned about the false negatives," Birnbaum says of the rapid screening. In environmental health, giving a clean bill of health to a substance that came up negative in a rapid screening test could cause public health headaches in the future, she says.

THOSE CONCERNED about public health, however, have moved beyond the question about the classic toxicity of a chemical: Will this substance make someone sick and, if so, at what dose? They are increasingly focused on substances that may disturb the body's endocrine functions.

Studies of chemicals suspected of being endocrine disrupters raise complex issues, Birnbaum explains.

"When you're dealing with hormonal activity, context is everything and interaction is everything. A given hormone in a given tissue at a given developmental stage may cause one thing to happen. The same hormone in another tissue or another development stage may cause exactly the opposite kind of thing to happen," Birnbaum says.

Scientific understanding of how the endocrine system works continues to evolve, she points out. "Twenty years ago, we knew that estrogen worked through a receptor. But now we know there isn't one estrogen receptor, there are multiple estrogen receptors," Birnbaum says. Plus, there are interactions. "We know

that the estrogen receptor, for example, doesn't act in isolation but interacts with other hormones and receptors," she explains.

Then there's the issue of hormonal variations among individuals, Birnbaum adds. For instance, if a given exposure to an endocrine-disrupting chemical decreases a man's testosterone by 10%, plenty of men would experience no effects, and their levels of this hormone would remain in the normal range. But this would not be the case for men who, before exposure, have testosterone levels on the lower end of the normal range.

Such complexities feed into public health policy and science policy debates, such as the one over bisphenol A (BPA). This chemical, which is used in polycarbonate bottles and epoxy-based food can liners, is an estrogen mimic. FDA is in the midst of a debate over whether it should allow continued use of BPA in food and beverage containers (C&EN, Nov. 17, 2008, page 42). In September 2008, the National Toxicology Program deemed BPA of "some concern" for developmental and behavioral effects in fetuses, infants, and children (C&EN, Sept. 8, 2008, page 28).

"There is not enough around to make a difference at the current levels you see in the human population," Birnbaum says of BPA. Yet BPA is one of more than two dozen chemicals people are exposed to that act as weak estrogen mimics, she continues. "They're all weak, but if you even just use a simple dose addition method, all of a sudden the total estrogenic activity is not insignificant," she adds.

Birnbaum points out that the endocrine system goes beyond the heavily studied estrogens, androgens, and thyroid hormones. "There are many other endocrine systems in our body that we need to consider," she says.

"We have a tendency in science to become experts about something very narrow. We're so focused on minutiae that we miss the big picture," she says. "Our bodies and our integrated systems are not simple. There are all the interactions between the parts."

This sort of understanding about parts integrating into a whole offers insight into how Birnbaum is approaching her post at NIEHS.

"The mission of NIEHS is to reduce and prevent environmental impact on disease," Birnbaum says. "It's not only the disease of the individual." Effects may be subclinical or difficult to detect in a given person, but they may affect the overall health of the population, she explains.

"If we can understand how a certain environmental chemical or environmental stressor causes a disease process," she says, researchers can work to stop progression of health problems, as well as prevent them.

Chemicals

Birnbaum On Dioxins' Toxicity, Regulation

Linda S. Birnbaum, the new director of the National Institute of Environmental Health Sciences, has spent a sizable chunk of her scientific career focused on dioxins, furans, and polychlorinated biphenyls. This family of chlorinated or brominated chemicals is commonly lumped together under the moniker "dioxins."

Birnbaum has witnessed how regulation has virtually eliminated production of these toxic chemicals over the past three decades.

"The major sources that were present in the '60s and '70s are no longer significant sources at all. The processes that created them are no longer being used" commercially, she says. Plus, studies show that the levels of dioxins are dropping both in the environment and in people's bodies.

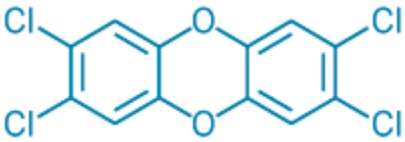
"That's the good news," Birnbaum says. "On the other hand, our continued scientific study of dioxins has revealed that they're much more toxic than we used to believe."

In the past, researchers were concerned about dioxins being lethal after short-term exposure. But nowadays, Birnbaum says, "we are concerned about their subtle developmental effects" and possible long-term cancer risks from exposure.

"For years, with dioxins, nobody really understood that they affected heart development. Well, we knew that it was true in fish, and we knew it was true in birds," she explains, "but nobody had ever really shown that it caused effects during mammalian development or in adults." That's because scientists weren't looking for these outcomes, she says. Now that researchers are probing the possibility of these effects, they are finding them.

In addition, dioxins are linked to an increase in type 2 diabetes. Age and obesity may be more important risk factors for this disease than dioxin exposure, Birnbaum says, but that doesn't make regulation of these substances irrelevant.

"You can't control your age. Many people are not very successful at controlling their weight," she says. "But we as a society can control our dioxin exposure."



INFAMOUS 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin is the most hazardous member of the family of chlorinated and brominated dioxins

To access video clip, refer to article http://pubs.acs.org/cen/government/87/8705gov1.html

Bloomberg.com
September 3, 2008
By Tom Randall

Chemical in Soda Cans, Baby Bottles May Harm Kids

Exposure to bisphenol A, a chemical used to make plastic for baby bottles and to line soda cans, may harm fetuses and children and needs further study before it is deemed safe, a U.S. government report found.

Tests in animals showed harmful effects from the chemical, known as BPA, the National Toxicology Program said today in a report that rated concern about the chemical's risks for children at the middle of a five-point scale. Parents may want to limit family exposure to the substance, said the study's authors, though they didn't recommend changing U.S. safety standards.

The study, the final version of a report issued in draft form in April, underscores differences within the government about the chemical's safety. The staff of the Food and Drug Administration said in a draft report last month that the agency ``has concluded that an adequate margin of safety exists'' for bisphenol A when used in products coming into contact with food.

``The possibility that BPA may affect human development cannot be dismissed,'' said John Bucher, associate director of the toxicology group, in a statement today. ``We see developmental changes occurring in some animal studies at BPA exposure levels similar to those experienced by humans.''

The National Toxicology Program, part of the Health and Human Services Department, was created in 1978 to provide scientific assessments of the health effects of chemical agents in the environment, according to the program's Web site.

The FDA's staff assessment also recommended more detailed testing, specifically in adult, pregnant and newborn monkeys, to look for effects on nervous system development and behavior. A subcommittee of the FDA's Science Board plans to review the agency's staff report at a Sept. 16 meeting in Rockville, Maryland.

Industry Response

``There is no direct evidence that exposure to bisphenol A adversely affects human reproduction or development,'' said the American Chemistry Council, which represents the chemical industry, in an e-mailed statement today. Evidence from animal studies was ``limited and inconclusive'' and ``additional research will be needed to determine if these concerns are relevant,'' the group said.

In April, Canada became the first country to label bisphenol A as ``toxic'' and is considering a ban on its use in baby bottles. U.S. lawmakers have considered similar proposals to prohibit use of the chemical.

``We should err on the side of caution and keep this chemical out of children's products,'' said Senator Charles Schumer, a New York Democrat, in an e-mailed statement today. ``Clearly more research is needed.''

Coca-Cola, PepsiCo

Bisphenol A is used to stiffen plastic used to make baby bottles and to seal canned food. Coca-Cola Co. and PepsiCo Inc. use it in cans to protect the drink from direct contact with the aluminum and to prevent spoilage, said Tracey Halliday, a spokeswoman for the American Beverage Association, a Washington- based trade group.

Coca-Cola and Pepsi, which referred questions about bisphenol A to the beverage association, don't use the chemical in soft drink and water bottles, Halliday said.

Several companies that produce plastic bottles, such as Energizer Holding Inc.'s Playtex Infant Care unit and Thermo Fisher Inc., the maker of Nalgene sports bottles, have stopped using the chemical in their new products because of the concerns.

Average infant exposures are about 2,000 times less than the FDA's safety level, and exposures among adults are 27,000 times lower, that agency's draft report said.

To contact the reporter on this story: Larry Liebert in Washington at lliebert@bloomberg.net

http://www.bloomberg.com/apps/news?pid=20601124&sid=aTt_RXlTAvUw&refer=home#

CHEMICAL & ENGINEERING NEWS

September 3, 2008
GOVERNMENT & POLICY

Bisphenol A Assessment Released

Debate over the safety of low-level exposure to the plastics chemical continues

Britt E. Erickson

Current levels of exposure to bisphenol A (BPA), a chemical used in making polycarbonate plastic bottles and epoxy-based canned food liners, are of "some concern" for developmental and behavioral effects in fetuses, infants, and children, according to a final assessment released on Sept. 3 by the National Toxicology Program. The report comes just weeks after FDA declared in a draft assessment that the estrogenic chemical is safe in food contact products such as baby bottles and infant formula cans (C&EN, Aug. 25, page 10).

NTP's Center for Evaluation of Risks to Human Reproduction, an interagency federal research program located on the campus of the National Institute of Environmental Health Sciences in Research Triangle Park, N.C., has been evaluating since December 2005 the potential for BPA to cause reproductive and developmental effects in humans. Last April, the group expressed its concerns over the chemical in a draft report, which led to an intense debate and a congressional investigation into the safety of BPA in consumer products (C&EN, June 2, page 36).

The final NTP assessment reaffirms the earlier concerns and points to the need for more research into the safety of BPA. "There remains considerable uncertainty whether the changes seen in the animal studies are directly applicable to humans, and whether they would result in clear adverse health effects," NTP Associate Director John R. Bucher said in a statement. "But we have concluded that the possibility that BPA may affect human development cannot be dismissed."

FDA says it will consider the NTP report as it finalizes its own BPA assessment for regulatory purposes. A public meeting is scheduled for Sept. 16 to discuss FDA's draft assessment.

http://pubs.acs.org/cen/news/86/i36/8636news3.html

CNNMoney.com
September 03, 2008: 10:19 AM EST

Government Health Experts Concerned BPA Affects Human Growth

WASHINGTON -(Dow Jones) - Government experts on Wednesday released a final report on the safety of a chemical used in plastic baby bottles, saying they have "some concern" the chemical is linked to health and developmental problems.

The chemical, bisphenol-A, or BPA, makes plastic hard and shatterproof, and is used in hundreds of consumer products from plastic baby bottles to CDs.

The report, released by the Department of Health and Human Services' National Toxicology Program, doesn't say BPA should be banned but that more research is necessary to understand how the chemical affects human health.

"There remains considerable uncertainty whether the changes seen in the animal studies are directly applicable to humans, and whether they would result in clear adverse health effects," said NTP Associate Director John Bucher, Ph.D." But we have concluded that the possibility that BPA may affect human development cannot be dismissed."

Concerns over the chemical's safety have heightened in recent months, prompting more than a dozen states to consider legislation banning BPA in some children and food products. Concerns about BPA also drove Wal-Mart Stores Inc. (WMT), among other retailers, to say it would stop selling baby bottles containing the chemical. Canada has said it intends to ban the use of BPA in baby bottles.

The Food and Drug Administration said last month, based on current science, that there isn't enough evidence to support banning the chemical from baby and food products. The agency's assessment relied on part of a draft of the report released today.

The FDA is holding a hearing on Sept. 16 to discuss BPA.

The report is similar to a draft the National Toxicology Program released in April. There are, however, a few key differences.

The final report says experts have "minimal concern" BPA exposure will affect the development of mammary gland or accelerate puberty in females. The draft said there was "some concern," which is a more elevated concern. Officials lowered the concern after a group of experts reviewing the draft said there wasn't enough evidence to support the earlier level of concern, said Michael Shelby, an associate director at NTP.

The NTP used a five-level scale of concern, ranging from negligible concern to serious concern. "Some concern" falls in the middle.

The NTP's report relies on a wide-array of research involving numerous laboratory studies, though most of the research was from academia, Shelby said.

The program's findings contradict some industry studies that say there is minimal concern BPA affects human development.

-- By Jared A. Favole, Dow Jones Newswires; 202.862.9207; jared.favole@ dowjones.com

http://money.cnn.com/news/newsfeeds/articles/djf500/200809031019DOWJONESDJONLINE000612_FORTUNE5.htm

Environment News Service

Bisphenol A May Affect Brain, Behavior, Prostate in Children

WASHINGTON, DC, September 3, 2008 (ENS) - Two federal government agencies are at odds over the safety of bisphenol A, a chemical used to harden plastic products such as baby bottles and drinking water bottles and for lining food and beverage cans.

A report today by the National Institutes of Health's National Toxicology Program finding that bisphenol A may alter brain development and behavior and increase the risk of prostate cancer in children, infants and fetuses is in direct contradiction to last month's assessment by the U.S. Food and Drug Administration that the chemical is safe at current levels of exposure.

Based on 261 scientific publications, the National Toxicology Program report contradicts an FDA draft report released in August which found that bisphenol A is safe at current human exposure levels and does not recommend banning the chemical.

Some 93 percent of Americans have detectable levels of bisphenol A in their urine, according to data from the Centers for Disease Control and Prevention on urine samples provided by 2,500 Americans aged six and older for a national health survey in 2003-2004.

The report released today was conducted by the National Toxicology Program based on the assessment of an expert panel convened by the Center for the Evaluation of Risks to Human Reproduction that evaluated the potential for bisphenol A to cause adverse effects on reproduction and development in humans.

Shatterproof baby bottles are often hardened with bisphenol A. (Photo by Wendy Lane)

The panel completed its evaluation in August 2007 and the NTP assessment also includes scientific information that has been reported since then.

CERHR Director Dr. Michael Shelby states in the report that bisphenol A was selected for evaluation because of widespread human exposure, public concern for possible health effects from human exposures, high production volume, and evidence of reproductive and developmental toxicity in laboratory animal studies.

After assessing the evidence, the National Toxicology Program said it has "some concern for effects on the brain, behavior, and prostate gland in fetuses, infants, and children at current human exposures to bisphenol A."

The NTP has "minimal concern for effects on the mammary gland and an earlier age for puberty for females in fetuses, infants, and children at current human exposures to bisphenol A."

The NTP has "negligible concern that exposure of pregnant women to bisphenol A will result in fetal or neonatal mortality, birth defects, or reduced birth weight and growth in their offspring."

The NTP has "negligible concern that exposure to bisphenol A will cause reproductive effects in non-occupationally exposed adults and minimal concern for workers exposed to higher levels in occupational settings."

The National Toxicology Program review reflects the findings of dozens of independent scientists from around the world who have raised questions about the chemical's possible dangers for more than a decade.

These plastic bottles do not contain bisphenol A. (Photo by Alicia Voorhees)

Richard Wiles, executive director of the nonprofit research organization Environmental Working Group, said today in a statement, "Unlike the FDA, NTP has listened to the nation's premier scientists and has concluded that the BPA threat to the brains, bodies and behavior of our children must be taken seriously."

"The agency's stance is measured and courageous in the face of the slick, relentless publicity campaign from the chemical industry, which seems to be following the tobacco industry's playbook," said Wiles.

He points out that the NTP reviewed several hundred independent scientific studies before reaching its conclusion, while the FDA relied on three chemical-industry funded reports, which gave the toxic chemical the thumbs up for use in consumer products.

"Consumers deserve straight talk from the government," said Wiles. "The new NTP assessment tells us that we are right to be concerned about BPA and the industry's ongoing chemistry experiment on our kids."

The American Chemistry Council, an industry trade group, today said it welcomes the release of the final report on bisphenol A from the National Toxicology Program, saying that the findings of the report identified no serious human health concerns.

"The safety of our products is our highest priority," said Steven Hentges, PhD, of the American Chemistry Council's Polycarbonate/BPA Global Group. "An earlier draft of the NTP report has already been used by the Food and Drug Administration to support their safety assessment, which confirms that food-contact products made from polycarbonate plastic, including products for infants and children, can continue to be used safely."

The FDA draft report, released August 15, states that based on lab tests in rodents, infants and adults are exposed to bisphenol A levels that are below toxic levels.

"Safe or safety means that there is reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use," but "complete certainty of absolute harmlessness is scientifically impossible to establish," the draft report states.

But Wiles said the FDA report "ignored the nation's top public health scientists, and instead lauded the benefits of a toxic, hormone disruptor found in virtually every infant in America."

http://www.ens-newswire.com/ens/sep2008/2008-09-03-093.asp

WebMD Health News
September 3, 2008

Bisphenol A: Some Concerns Remain

National Toxicology Program Notes Concerns in Final Bisphenol A Safety Report

By Miranda Hitti
Reviewed by Louise Chang, MD

Government scientists today expressed some concern about the plastic chemical bisphenol A -- but about fewer health topics than they noted last spring.

Bisphenol A, also called BPA, is found in polycarbonate plastic, including some water bottles and baby bottles, and in epoxy resins, which are used to line metal products, including canned foods.

Bisphenol A has been in the media spotlight since April, when the National Toxicology Program (NTP) issued a draft report expressing certain concerns about bisphenol A.

Since then, several major companies -- including Wal-Mart, Toys "R" Us, and Babies "R" Us -- have backed away from baby bottles containing bisphenol A, and Nalgene ditched bisphenol A in its consumer bottles.

But the plastics industry has steadily maintained that bisphenol A is safe for people at typical levels of exposure, and an FDA draft report, issued last month, agrees.

Now, the debate has come full circle, with today's release of the NTP's final report on bisphenol A. The plastics industry praises the report, saying it identified "no serious human health concerns."

But some NTP officials aren't so sure that their report settles all the questions about bisphenol A's safety. And the nonprofit Environmental Working Group continues to voice concern about bisphenol A, calling the NTP's report "courageous."

Bisphenol A Report

The NTP's final report on bisphenol A notes:

- "Some concern" for effects on the brain, prostate gland, and on behavior in fetuses, infants, and children.
- "Minimal concern" for effects on the mammary gland and an earlier age for puberty for females in fetuses, infants, and children, and for reproductive effects in adults who work with bisphenol A.
- "Negligible concern" for fetal or neonatal death, birth defects, or reduced birth weight and growth in babies born to women exposed to bisphenol A during pregnancy, and also for reproductive effects in adults who don't work with bisphenol A.

In April, the NTP's draft report mentioned "some concern" for bisphenol A's effects on mammary glands and early female puberty. In June, an NTP advisory panel recommended changing that to "minimal" concern, and the NTP followed that advice in its final report.

NTP's Lingering Questions

Much of the research on bisphenol A's safety has been done on animals, and NTP officials say it's not clear how that translates to people.

"There remains considerable uncertainty whether the changes seen in the animal studies are directly applicable to humans, and whether they would result in clear adverse health effects," NTP Associate Director John Bucher, PhD, says in a news release. "But we have concluded that the possibility that BPA may affect human development cannot be dismissed."

So what does the NTP recommend that consumers do?

"Unfortunately, it is very difficult to offer advice on how the public should respond to this information," Michael Shelby, PhD, director of the NTP's Center for the Evaluation of Risks to Human Reproduction (CERHR), says in a news release.

"More research is clearly needed to understand exactly how these findings relate to human health and development, but at this point we can't dismiss the possibility that the effects we're seeing in animals may occur in humans. If parents are concerned, they can make the personal choice to reduce exposures of their infants and children to BPA," Shelby says.

Plastics Industry, Critics Respond

All along, the American Chemistry Council, a trade group for the plastics industry, has maintained that bisphenol A is safe at typical exposure levels, and that lab tests on animals aren't a good gauge of risk to humans.

That's in line with the FDA's draft report and a separate report by European health officials concluded in July. And in August, California lawmakers rejected a bill that would have limited bisphenol A to trace amounts in products geared to kids aged 3 and younger.

"The safety of our products is our highest priority," Steven G. Hentges, PhD, of the American Chemistry Council's Polycarbonate/BPA Group, says in a news release. "An earlier draft of the NTP report has already been used by the [FDA] to support their safety assessment, which confirms that food-contact products made from polycarbonate plastic, including products for infants and children, can continue to be used safely."

Meanwhile, the EWG focuses on the concern mentioned in the NTP's report, calling it a "measured" stance. In a statement emailed to WebMD, EWG Executive Director Richard Wiles is critical of the plastics industry and the FDA, and says "the new NTP assessment tells us that we are right to be concerned about BPA."

The NTP's report is about science. It doesn't make recommendations about banning or otherwise regulating bisphenol A; that's up to the FDA. An FDA spokesperson wasn't immediately available to comment on the NTP's final report.

http://www.webmd.com/news/20080903/bisphenol-a-some-concerns-remain

Associated Press
By Matthew Perrone
September 4, 2008

Plastic chemical still concerns toxicologists

The FDA calls bisphenol A safe. Some say it may cause trouble in the brain, hormonal systems.

WASHINGTON - Government toxicologists have reiterated safety concerns about a chemical used in baby bottles and food containers, just weeks after the Food and Drug Administration declared the substance safe.

A report issued yesterday said there was "some concern" that bisphenol A can cause developmental problems in the brain and hormonal systems of infants and children.

The conclusion from the National Toxicology Program repeats initial findings issued in April. The group, with scientists from the National Institutes of Health and other agencies, said bisphenol's risks to humans cannot be ruled out, but acknowledged that its concerns are based on animal studies.

The American Chemistry Council, which represents plastics manufacturers, stressed that studies from animals provided "limited and inconclusive evidence." The group has spent the last year defending the safety of bisphenol from new concerns about the risks to children.

'More research'

Bisphenol A is a plastic-hardening chemical used to seal canned food and make baby bottles. After more than a year of complaints from consumer and parent groups, the FDA has agreed to revisit the chemical's safety. The agency last month said the trace amounts that leach out of food containers were not a threat to children or adults.

The toxicology group said that might not be true.

"More research is clearly needed to understand exactly how these findings relate to human health and development," said Michael Shelby, who directed the group's report. "But at this point we can't dismiss the possibility that the effects we're seeing in animals may occur in humans."

The FDA said it would consider the new report as it continued reviewing bisphenol. The agency has scheduled a meeting later this month where its outside advisers will weigh in on the chemical's safety. A final report is expected later in the year.

The toxicology group did back away from one issue raised in its draft. While the group said in April that there was "some concern" the chemical could speed up puberty in girls, the final report states there is now only "minimal concern" about those risks.

The National Toxicology Program ranks its conclusions about chemical risks on a five-tiered scale ranging from "negligible concern" to "serious concern."

Major retailers

Shelby said it was too early to recommend changes in what consumers buy and eat, but he added that parents who are concerned can avoid buying food containers made from bisphenol.

Several major retailers - including Wal-Mart and Toys R Us - have said they would stop selling baby bottles made with the chemical next year. And smaller companies like Evenflo and BornFree have ramped up production of glass baby bottles as an alternative.

Canada has said it intends to ban the use of the chemical in baby bottles. Lawmakers in several states and in Congress have introduced bills to ban it in children's products.

http://www.philly.com/philly/news/nation_world/20080904_Plastic_chemical_still_concerns_toxicologists.html?adString=ph.news/nation_world;!category=nation_world;&randomOrd=090408052600

WashingtonPost.com

Chemical in Plastic Is Connected to Health Problems in Monkeys

By Lyndsey Layton
Washington Post Staff Writer
Thursday, September 4, 2008; A02

Researchers at the Yale School of Medicine have linked a chemical found in everyday plastics to problems with brain function and mood disorders in monkeys -- the first time the chemical has been connected to health problems in primates.

The study is the latest in an accumulation of research that has raises concerns about bisphenol A, or BPA, a compound that gives a shatterproof quality to polycarbonate plastic and has been found to leach from plastic into food and water.

The Yale study comes as federal toxicologists yesterday reaffirmed an earlier draft report finding that there is "some concern" that bisphenol A can cause developmental problems in the brain and hormonal systems of infants and children.

"There remains considerable uncertainty whether the changes seen in the animal studies are directly applicable to humans, and whether they would result in clear adverse health effects," John R. Bucher, associate director of the National Toxicology Program, said in a statement. "But we have concluded that the possibility that BPA may affect human development cannot be dismissed."

In a study published in the Proceedings of the National Academy of Sciences, the Yale team exposed monkeys to levels of bisphenol A deemed safe for humans by the Environmental Protection Agency and found that the chemical interfered with brain cell connections vital to memory, learning and mood.

"Our findings suggest that exposure to low-dose BPA may have widespread effects on brain structure and function," the authors wrote. In contrast to earlier research on rodents, the Yale researchers studied monkeys to better approximate the way BPA might affect humans.

"Our goal was to more closely mimic the slow and continuous conditions under which humans would normally be exposed to BPA," said study author Csaba Leranth, a Yale professor of obstetrics, gynecology and reproductive sciences and of neurobiology.

BPA, in commercial use since the 1950s, is found in a wide variety of everyday items, including sports bottles, baby bottles, food containers and compact discs. One recent federal study estimated that the chemical is found in the urine of 93 percent of the population.

The American Chemistry Council, a trade group, maintained yesterday that "there is no direct evidence that exposure to bisphenol A adversely affects human reproduction or development."

The National Toxicology Program, part of the National Institutes of Health, has no power to regulate BPA, but its findings are used by other federal agencies such as the Food and Drug Administration and the EPA, which set safe exposure limits for chemicals.

The FDA plays a critical regulatory role because it regulates the compound's use in plastic food containers, bottles, tableware and the plastic linings of canned foods.

The agency last month issued a draft report that declared BPA safe for use in food packaging and bottles, based largely on the strength of two studies, both funded by industry.

"Unfortunately the regulatory agency charged with protecting the public health continues to rely on industry-based research to arrive at its conclusions, rather than examining the totality of scientific evidence," Rep. John D. Dingell (D-Mich.), chairman of the House Energy and Commerce Committee, said in a statement yesterday. His committee is investigating the FDA's handling of BPA.

U.S. manufacturers make about 7 billion pounds of BPA annually. A ban would affect thousands of businesses and perhaps billions of dollars in profit for its largest manufacturers.

Canada has said it intends to ban the use of BPA in baby bottles, and state and federal lawmakers have proposed a variety of BPA bans. Sen. Charles E. Schumer (D-N.Y.) is sponsoring a bill to prohibit BPA from children's products, while Rep. Edward J. Markey (D-Mass.) wants to bar it from all food and drink packaging.

"The FDA's assurances of BPA's safety are out of step with mounting scientific evidence to the contrary," Markey said yesterday. "For the sake of the health of every man, woman and child in America, we should ban BPA in food and beverage containers, especially because there are alternatives already available."

Several major retailers, including Wal-Mart and Toys R Us, have pledged to drop BPA products next year while some makers of baby bottles and sports bottles have switched to BPA-free plastic.

http://www.washingtonpost.com/wp-dyn/content/article/2008/09/03/AR2008090303397_pf.html

The New York Times
nytimes.com

September 6, 2008

EDITORIAL

That Plastic Baby Bottle

What do you do when one arm of the government says everything is O.K. and another tells you to watch out? That is what is happening with bisphenol-A — a chemical used in many plastics and epoxy resins now found in baby bottles and liners for canned goods. The answer is a truism in every family rulebook — when in doubt, especially when it comes to children, err on the side of caution. That means it is a good idea to keep the young away from bisphenol-A, or BPA.

The Food and Drug Administration said last month that the small amounts of BPA that leach out of containers and into food or milk are not dangerous. Then this week, the National Toxicology Program, the federal agency for toxicological research, reported that their research shows "some concern" about the effects of BPA on the brain development and behavior of fetuses and young children.

A new study by the Yale School of Medicine is cause for even more concern. In tests on primates, researchers found that BPA "causes the loss of connections between brain cells" that could cause memory or learning problems and depression.

John Bucher, the associate director of the toxicology program, said there is still considerable uncertainty about whether the changes seen in animal studies are causing the same problems in humans. "But we have concluded that the possibility that BPA may affect human development cannot be dismissed."

Scientists from the toxicology offer this advice:

- Watch for the numeral 7 on the bottom of plastic containers. That often means they contain BPA.
- Don't microwave plastic food containers made with BPA. Better to use glass or porcelain.
- Watch out for canned foods for children.
- Search for baby bottles and other baby products that are BPA-free.

Some states are considering bills to restrict the use of BPA for the young, and Congress is assessing several possible remedies including a BPA ban in children's products or a ban on BPA in packaging that touches food. The best effort, however, would be the Kid-Safe Chemicals Act. It would require that children's products are proved safe before they are sold, not — as with BPA — the other way around.

http://www.nytimes.com/2008/09/06/opinion/06sat4.html

TIME
IN PARTNERSHIP WITH CNN
Monday, Sep. 15, 2008

Concerns About Chemical in Plastics

By Bryan Walsh

For years, a small but growing band of scientists has been raising concerns about the impact on human health of bisphenol A (BPA), a chemical used in plastic that mimics the effect of the hormone estrogen. BPA can be found in a wide variety of products, including some plastic bottles and the lining of aluminum cans, and it can migrate fairly easily into the human bloodstream. That means few of us escape exposure, if in small doses — in one survey, 93% of Americans tested positive for the chemicals. Concerned researchers point to animal studies that indicate that even low-dose exposure to BPA may be associated with a variety of ills, including cancer and reproductive problems. But defenders — most prominently the chemical industry itself — argue that the average dose of BPA is far too low to be toxic, and that in any case, there have never been human studies implicating the chemical as dangerous. So far that argument has carried the day — the Federal Drug Administration (FDA) last month announced that the BPA wasn't dangerous to human health in small doses, and declined to regulate it.

The science may be changing, however. In a study published Sept. 16 in the *Journal of the American Medical Association (JAMA),* a group of researchers led by David Meltzer of the University of Exeter in Britain reviewed data from the U.S. government's comprehensive National Health and Nutrition Examination Survey, looking for any connections between BPA exposure and health problems. They found more than a few. The *JAMA* study indicates higher levels of BPA in urine — the simplest way to test for the chemical — was associated with higher incidences of cardiovascular disease, diabetes and liver enzyme abnormalities. The article represents the first large-scale study of BPA in a human population — and is sure to add to the controversy surrounding it. "This isn't just any old epidemiological study — this is a national survey," says Frederick vom Saal, a biologist at the University of Missouri and an outspoken opponent of BPA, who wrote an editorial accompanying the *JAMA* study. "This carries greater weight."

Compared with the quarter of the surveyed population (aged 18 to 74) with the lowest levels of BPA, the quarter who had the highest levels were more than twice as likely to report having cardiovascular disease or diabetes. But the study's authors take pains to point out that their research does not prove that BPA can cause these ills, but merely indicates that these disorders seem to occur more often in people with higher levels of the disease. To prove a cause-effect relation would require longitudinal studies that compare the effects of BPA in one group to a control group unexposed to the chemical — hard to do, given BPA's ubiquity. But the *JAMA* study is worrying enough. "The article says that the more of this chemical you have, the greater the risk," says vom Saal. "We understand how BPA causes these problems in animals, and the human study follows that." A recent study by the Yale School of Medicine provides even more cause for concern, showing that tests in primates found that BPA "causes the loss of connections of brain cells" that could lead to memory problems, and even depression.

Though the FDA has ruled BPA safe, not everyone in the government agrees. Earlier this month the National Toxicology Program (NTP), a federal agency that gauges the safety of chemicals, reported that its research shows "some concern" about the effects of BPA on the brain development of fetuses and young children. (Children are considered particularly vulnerable to the chemical, which is thought to interfere with development.) Critics note that the FDA's report relied on a small number of studies funded by industry groups that manufacture BPA, while the NTP took in a wider range of science. "The FDA says that their safety standard is that there must be reasonable certainty among competent scientists that a chemical is not harmful," says vom Saal. "So unless they declare the NTP scientists incompetent, something is wrong here."

Vom Saal and other scientists will have a chance to have their voices heard on Sept. 16, when the FDA convenes an open meeting to reassess the safety of BPA. Other governments have already moved to regulate the chemical, including Canada, which has considered banning it. For concerned parents, limiting BPA exposure for children isn't that hard. Watch out for the number 7 on the bottom of plastic containers, which often means they contain BPA; avoid canned foods for children; and don't microwave plastic food containers that contain the chemical, as heat can make it easier for BPA to leach. Ultimately, though, it may not even matter what the FDA does — a new report by the Investor Environmental Health Network says that consumers, manufacturers and retailers are already forgoing the chemical, buying and selling BPA-free bottles and other products. Wal-Mart and Toys 'R Us have already announced their intention to shift away from products containing BPA. Which shouldn't be surprising — in America, commerce leaves science and the government in the dust.

http://www.time.com/time/printout/0,8816,1841441,00.html

TIME
IN PARTNERSHIP WITH CNN

Reassessing the Dangers of BPA in Plastics

Sunday, Nov. 02, 2008
By Alice Park

There's no denying that bisphenol A (BPA), the latest headline-making toxin, is ubiquitous — it's in hard plastic water bottles, the lining of food and beverage cans and, most disturbingly, the plastic baby bottles that most parents commonly use. What's less clear, however, is exactly what effect BPA has on human health.

That was the subject of an Oct. 31 daylong meeting of the Food and Drug Administration's (FDA) Science Board. Earlier last week a panel commissioned by the Science Board released its review of the FDA's safety report, which concluded in August that current levels of BPA exposure posed no real health risk. The Science Board convened Friday to discuss the panel's findings — a highly critical 17-page review that deemed the FDA's conclusions flawed — and to hear comments from the public about whether the compound should be banned from food and beverage containers. The board will now forward the review along with the FDA's original safety assessment to FDA chief Dr. Andrew von Eschenbach. The FDA has until February 2009, when the Science Board next meets, to respond.

Why the renewed uproar over plastic? Since the FDA completed its original analysis in August, additional data on the potential health effects of BPA have emerged, linking high levels of BPA exposure to increased risk of heart disease and diabetes and even a decreased sensitivity to chemotherapy in cancer patients. The compound is also linked to developmental and brain effects in infants; BPA is known to mimic the hormone estrogen in the body, which can cause changes in developing fetuses and infants. "There is enough evidence today for the FDA to take the precaution and to certainly get BPA out of infant products," says Urvashi Rangan, senior scientist and policy analyst at Consumers Union. "Even more, consumers should not be ingesting this substance while the science is being figured out."

The FDA's initial assessment — which it has not rescinded — that "an adequate margin of safety exists for BPA at current levels of exposure from food-contact uses, for infants and adults" was based on data available at the time. Back in April, for example, the National Toxicology Program, which is part of the National Institutes of Health (NIH), released a preliminary report expressing "some concern" that according to studies done in animals, BPA could have neural and behavioral effects on fetuses, infants and children at current levels of exposure. Recent surveys by the Centers for Disease Control and Prevention (CDC) had suggested that exposure is widespread, showing that 93% of Americans excrete some BPA in their urine. Still, the weight of the evidence, mostly from animal studies, did not suggest a significant health risk in humans, according to the FDA.

But last week, the reviewing panel disagreed, saying the FDA's analysis excluded several important studies on BPA in animals. The panel also questioned the quality of some of the included studies and found that the FDA did not incorporate enough infant-formula samples in its evaluation. According to the panel review, the FDA's safety report "creates a false sense of security" and the agency's margins of safety for BPA exposure are, in fact, "inadequate." Says Tracey Woodruff, director of the program on reproductive health and the environment at the University of California, San Francisco, and a former Environmental Protection Agency scientist: "Unless the evidence is very compelling, you don't get such a strong statement from a group of scientists."

It's now up to Von Eschenbach to decide how to proceed. He may start from scratch and commission another report that includes the most recent findings on BPA; he may reject the panel's review and adhere to the FDA's original conclusion that BPA is harmless at current exposure levels; or he may ban the chemical from baby products, as the Canadian government did in April. Or he may draw no further conclusions about BPA until additional studies can be commissioned and completed to answer some unresolved questions.

"While we have some idea of how much BPA might leach from a baby bottle, there are intermediate steps between that and how much gets into an infant that we still need to model and establish mathematically," says John Bucher, associate director of the National Toxicology Program, which collaborates with the FDA, NIH and CDC. "And we don't have that yet." The FDA report maintains, for example, that a BPA exposure level of 5 mg/kg per day is acceptable. Health officials have determined that baby bottles can produce anywhere from 7 micrograms/g to 57.7 micrograms/g of BPA. The questions are: How much of the compound is absorbed into an infant's body? How much remains, and how much is excreted? And does that exposure come close to the FDA threshold?

The FDA can't answer those questions yet, but some experts argue that the agency doesn't need to wait to take action. "The Federal Government entered into a voluntary recall of the Teflon chemicals [in pots and pans] on less evidence than we have for BPA," says Woodruff, "because there was concern that people were chronically exposed to a chemical linked to some evidence of potential human harm." Woodruff says the estimated range of exposure to BPA for formula-fed infants is within the range of doses that have led to adverse effects in animal studies.

Until the government settles on a new assessment or action, experts say parents have the option of using BPA-free products — including glass, stainless steel and some innovative next-generation plastics that do not contain the chemical.

http://www.time.com/time/health/article/0,8599,1855853,00.html

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EDITORIAL

A Flawed Assessment of BPA

After reports of a possible conflict of interest, we worried that a scientific advisory panel might pull its punches in evaluating the Food and Drug Administration's judgments on the safety of bisphenol-A, known as BPA. It didn't.

In a devastating new report, the panel charged that a draft safety assessment prepared by the F.D.A. ignored relevant studies, used flawed methodology and created "a false sense of security" about the safety of BPA, which is found in baby bottles, plastic water bottles and the liners of cans, among other products.

The draft assessment had concluded that the small amounts of BPA that leach into milk or food are not dangerous. The advisory panel did not directly dispute this. But it left little doubt that the weight of the evidence, in its view, suggests the need for a much greater safety margin than the F.D.A. draft deemed adequate.

The United States National Toxicology Program — which considered many of the studies the F.D.A. had discounted — has expressed some concern about BPA's safety, and Canada has moved toward banning the sale of baby bottles made with BPA. Some research suggests that BPA might cause neurological damage, accelerate puberty, interfere with chemotherapy and increase the risk for heart disease, diabetes and cancer.

The F.D.A.'s Science Board, an advisory group, endorsed the panel's critique on Friday. Now it is imperative that the F.D.A. complete a more rigorous assessment. It must also consider whether to restrict some uses of BPA without waiting for further research.

http://www.nytimes.com/2008/11/01/opinion/01sat3.html

December 30, 2008

Top health stories of '08: Stress, drugs and chemical lows

The following is one of the stories listed in this article …

Public, Congress examine chemicals in kids' products

People took a closer look at the plastic in their children's toys and baby bottles this year, as scientists, lawmakers and regulators debated the safety of hormone-like chemicals that were unknown to most Americans a year or two ago.

•In August, Congress passed a sweeping product-safety law to dramatically lower the amount of lead in products for children under 12 and virtually ban six types of phthalates, hormone-like chemicals that are used to soften plastic and have been linked to reproductive changes in boys. The law takes effect Feb. 10 (full story).

•In September, the National Toxicology Program expressed "some concern" about the effects of another plastic ingredient, bisphenol A, or BPA, on the development of the brain and prostate in children and fetuses. The ingredient has also been linked to behavioral issues in young children.

•In October, Canada declared BPA to be toxic and announced plans to ban its use in baby bottles.

Also in October, an advisory panel to the Food and Drug Administration harshly criticized the agency, which says that BPA is safe at the level to which people are commonly exposed (full story). The outside panel says the FDA ignored important evidence, including studies that suggest babies are at risk. Although the FDA says it's committed to additional research, the agency hasn't changed its opinion on BPA's safety.

The marketplace, however, responded quickly to these concerns.

In anticipation of Canada's decision, most baby-bottle makers now sell BPA-free alternatives. Makers of liquid infant formula say they're looking for alternatives to BPA, which they now use to line their metal cans. Retailers such as Wal-Mart, CVS and Babies R Us also are phasing out BPA.

— By Liz Szabo

http://www.usatoday.com/news/health/2008-12-28-year-medical_N.htm

GLAMOUR

The Scariest Health Threat You've Never Heard Of

September 2008 Issue
by Donna Jackson Nakazawa

Early in 2004 Erin Farley, 26, began to suffer from fatigue, fevers, dizziness and joint pain. "It was so bad that shaking hands was excruciating," she says. "I couldn't open a jar or a car door; I couldn't even button my pants. I just didn't have the strength." Eventually the pain became so intense that she couldn't get out of bed. Newly married, she and her husband spent the better part of their honeymoon year dealing with her illness: "He'd brush my hair, dress me, cook what food I could swallow." Farley went from doctor to doctor in search of answers, and finally, a year and a half after she first noticed her symptoms, was diagnosed with rheumatoid arthritis, an autoimmune disease. A family of nearly 100 conditions, autoimmune diseases strike when the body's immune system, which is meant to protect you from foreign invaders such as bacteria and viruses, mistakenly turns on your own organs and systems; in rheumatoid arthritis sufferers like Farley, the joints and tissues are under attack.

It took three years, and Farley now has some control over her health. Still, she remembers the baffling period before her diagnosis as one of the worst times in her life. "No one, not even your friends, really understands what you're going through," she says. "People aren't *trying* to be mean, but if your doctors don't understand what's happening to you, it's no surprise that other people may think you're making it up."

Stories like Farley's are strikingly common among young women with autoimmune disease. For seven months Kathy Curran, 28, experienced severe tingling in her arms, recurrent migraines, blurred vision and even one scary episode of momentary blindness—but doctors "said my symptoms were just pinched nerves," she says. An MRI and a spinal tap finally gave a name to her ailment: multiple sclerosis (MS), which causes the immune system to attack the central nervous system and can lead to paralysis. Since then, she says, "it seems as soon as I tell someone I have MS, they always say, 'Oh! I just found out that my friend's sister has that too!'"

Melissa Weissman, 24, had similar terrifying vision problems along with a sensation of pins and needles down her back. When tests delivered a verdict of MS, it felt surreal: Three of her friends, all women between the ages of 25 and 35, had recently been diagnosed with autoimmune diseases, including type 1 diabetes, in which the immune system attacks insulin-producing cells in the pancreas. "It already seemed odd to me that so many young women I knew were being diagnosed with diseases in which the body basically turns against itself," Weissman says. "I just never thought that I could be one of them."

Katie Hall was 19 when her excruciating stomach pains led to the diagnosis of ulcerative colitis, in which the immune system attacks the lining of the intestines. Her best friend suffers from rheumatoid arthritis. "We always talk about how bizarre it is that two young, confident college girls like us could be hit by autoimmune diseases out of the blue," says Hall, now 21. They weren't an atypical pair; when she went to the hospital for treatment, she was shocked to see that "so many patients sitting in the IV infusion chairs were women my age. I just don't get it. Why?"

These young women are the living faces of what many scientists call an alarming trend. Rates of autoimmune diseases have been climbing rapidly over the past four decades. These illnesses now afflict an estimated 23.5 million Americans—78 percent of whom are female. That means that more than 18 million women in this country are living with an autoimmune disease, compared with 2.4 million with breast cancer. Why are women more at risk than men? "We suspect that estrogen may cause our immune systems to produce more antibodies, which are meant to protect us, but may make it more likely for the body to turn on itself," says DeLisa Fairweather, Ph.D., assistant professor in the division of toxicology at the Johns Hopkins Bloomberg School of Public Health's department of environmental health sciences.

Experts say that some of the increase in these diseases is really an increase in diagnoses—but that the climb is too dramatic to attribute to that alone. “Although the research in this area is limited, many autoimmune diseases appear to be steadily on the rise,” says Fred Miller, M.D., Ph.D., chief of the environmental autoimmunity group at the National Institute of Environmental Health Sciences. “That’s in contrast to rates of many other illnesses that have remained flat or even decreased.”

Doctors are seeing the trend play out in exam rooms every day. “Autoimmune diseases such as MS and transverse myelitis [a similar disease] used to be rare disorders. Now estimates show there may be 400,000 people with MS in the United States alone,” says Douglas Kerr, M.D., director of the Transverse Myelitis Center at Johns Hopkins. “Most of the patients we’re now seeing are young, previously healthy women. We’re facing an epidemic of autoimmune disease—one that we need to recognize now.”

Despite the mounting evidence, talking about the autoimmune epidemic today is a bit like talking about global warming before *An Inconvenient Truth* was released. Ninety-four percent of people can’t name a single autoimmune disease, according to one study, and many doctors haven’t fully educated themselves on how to diagnose these conditions. As a result, most autoimmune patients see four doctors over four years before they receive a diagnosis. Kathleen Arntsen, president of the Lupus Foundation of Mid and Northern New York, was in her early thirties when she began suffering from severe muscle fatigue and disabling weakness. She was told dismissively by a doctor, “We’ve given you every test known to man except for an autopsy. Would you like one of those, too?” It was five years before Arntsen received the diagnosis of myasthenia gravis, an autoimmune disease that destroys the nerves’ ability to stimulate and control muscle action. “Young women are so often treated like fruitcakes when they fall ill with these diseases,” Arntsen says. “Meanwhile, their entire lives are turned upside down.”

Thankfully, researchers have begun to slowly unlock key findings about autoimmune disease. “These diseases all begin the same way—something triggers the immune system to attack your own body,” says Fairweather. What flips the switch? Signs increasingly point to environmental factors such as the food we eat, the levels of stress we live with and the pollutants our immune systems are exposed to. No one factor is deadly; in most cases it’s likely that the cumulative buildup of many environmental problems poses health risks. “Even though you may have the same genetic tendencies as your mother or grandmother, today’s environment is more likely to pull the trigger that makes you get sick,” explains Pamela Peeke, M.D., author of *Body for Life for Women* and a former senior research fellow specializing in integrative medicine at the National Institutes of Health.

The best analogy is the age-old idea of the straw that broke the camel’s back: Your immune system can function under even a heavy load of environmental stressors. But one too many and it completely breaks down. What are the most common straws for young women? And how can *you* stay safe? Experts are beginning to understand exactly that.

Our Junk Food Ways

“Today’s highly processed food diet is a contributor to the autoimmune epidemic,” says Gerard Mullin, M.D., director of integrative gastroenterology nutrition services at the Johns Hopkins Medical Institutions. He cites the refined carbs and dangerous fats found in many processed foods, as well as the lack of fiber, antioxidants and phytonutrients. How does what’s in your stomach affect your immune system? “The lining of the gut is on alert for any strange stuff we’re eating,” says Dr. Peeke. “The body has to decide at that moment, ‘Do I digest that, absorb that or get rid of it right away?’ If the food is, say, a whole food like broccoli, the gut doesn’t give a damn, and it’s quickly digested. But spray that broccoli with pesticides, and the gut says, ‘Now you’ve got my attention.’ And the immune system has to go to work.” Recent studies show that when immigrants from South Asian countries move to Western countries and likely begin to eat processed food diets, they have an increased incidence of autoimmune diseases such as Crohn’s and ulcerative colitis. Studies like this haven’t been the only thing to sway Dr. Mullin, whose own autoimmune disease, a rare condition called arachnoiditis, once nearly paralyzed him. “I’ve been extra vigilant about eating a whole foods diet,” he says—and his health has improved as a result. On his and most experts’ good-to-eat list: skinless chicken; low-mercury wild fish such as flounder and tilapia; vegetables; fresh fruits; whole grains from gluten-free sources; nuts; and olive and flaxseed oils. On the

not-good list: highly processed foods, including preserved bread products and cereals, preserved meats and other foods that are often full of chemicals, preservatives and additives. Sufferers should eat them rarely, if at all.

Dietary changes helped Angela Doss. Last December Doss, 28, was suffering from severe thirst, dizziness and fatigue—and had lost almost 20 pounds in three weeks. She says a doctor told her, “You just need to gain some weight. Go have a banana split and you’ll be just fine.” She was later rushed to the emergency room, where physicians diagnosed Doss—who was in a near-diabetic coma—with type 1 diabetes. In addition to daily insulin shots, “now I eat as many organic vegetables and fruits as I can,” Doss says. “I grew up on a fast-food diet of fried foods—Oklahoma meat and potatoes. It took me a while to learn to eat whole foods. But I’ve noticed a big difference in how I feel.”

Should we all cut back on junk? Yes, say experts like Dr. Peeke, who argue that doing so may help the average American woman cut her risk of contracting autoimmune disease. “People say we don’t have perfectly wonderful data yet, but come on,” says Dr. Peeke. “The best thing to do is to eat whole foods.”

Our 24/7 Stress Habit

If you’re skeptical that emotional issues can have real physical consequences, consider this: Parents who have suffered the loss of a child are 50 percent more likely to develop MS than those who’ve never gone through that trauma, according to one 2004 study. “Chronic stress has a toxic effect on almost every single tissue in the human body,” explains Dr. Peeke. “The immune system puts up the best front it can, but after being beaten up enough, it can no longer optimally protect you.” MS and rheumatoid arthritis are both associated with stressful life events, but it doesn’t take personal tragedy to raise your risk of autoimmune disease—being chronically stressed can also alter the immune response. And perhaps not surprisingly, women today seem to be more stressed than in generations past, says Robin Goland, M.D., an endocrinologist and codirector of the Naomi Berrie Diabetes Center at Columbia University Medical Center. “Today, we’re trying to do everything,” she says. “You have to be a little selfish to be healthy, and that’s hard for women.” If you’re chronically stressed, or, as Dr. Peeke says, “feeling helpless, hopeless or defeated,” finding an outlet is critical. “You can’t avoid stress; we need some in order to grow and evolve,” she says. “But you have to eliminate the stuff that wears you down, the stuff you ruminate about, as best you can.” Exercise, yoga or meditation are prime choices, since they can help steady stress hormones, but anything that breaks up your daily grind is beneficial.

Our Chemical World

Environmentalists talk about the carbon footprint we’re leaving on our planet; some health experts say we should also look at the chemical imprint we’re leaving within our own bodies. And many agree that our day-to-day exposure to pollutants, pesticides, heavy metals and chemicals is, in Dr. Kerr’s words, “a significant contributor to today’s rising rates of autoimmune disease.”

How can those pollutants have such an impact? It takes the human body thousands of years to adapt to new environmental stresses, explains Ahmet Hoeke, M.D., Ph.D., associate professor of neurology and neuroscience and director of the neuromuscular division at Johns Hopkins. “We’ve outpaced our evolutionary ability to keep up with the number of chemicals we come into contact with every day,” he says. And those numbers are huge: In 2005 the Centers for Disease Control and Prevention reported that when they sampled 2,500 people across the country to look for the “body burden,” or amount of chemicals each individual was carrying, they found traces of all 148 chemicals and pollutants they tested for, including PCBs, insecticides, dioxins, mercury and cadmium, which are toxic in higher doses.

Not all experts believe our polluted world makes us sick—some proponents of the “hygiene hypothesis” argue it’s too *clean*, believing that our germ-free homes and childhood vaccinations have eliminated the natural challenges to our immune systems that once taught our bodies how to defend us properly. But many specialists and some research dispute this idea; studies have found no link between infections, vaccinations and the diagnosis of type 1 diabetes, for example.

Still other critics refute the idea that chemicals might make us sick at all. “Just because we can measure a chemical in the blood doesn’t therefore mean it’s harmful,” says Jeff Stier, spokesman for the American Council on Science and Health (ACSH), a group that gets about 40 percent of its financial support from industry sources. (The ACSH says these are no-strings-attached donations.) “People want to be able to blame chemicals where they don’t have another explanation for the cause of a disease. I think we need more psychologists rather than more toxicologists.” The ACSH argues that we should focus on the things we know will improve health. “There are so many things we can do to protect ourselves—get good nutrition, quit smoking, buckle up,” says Stier.

Doubtless those universal guidelines are important, but an increasing number of researchers say possible chemical risks shouldn’t be ignored. “The people who first studied the connection between cigarette smoking and lung cancer faced the same criticism,” says Kathleen Gilbert, Ph.D., an associate professor in the department of microbiology and immunology at the Arkansas Children’s Hospital Research Institute in Little Rock, who has studied autoimmune diseases. “The only reason these things are ‘obvious’ now is because scientists decided to study them. Surely we owe it to the folks with autoimmune diseases to investigate.” Some research, Gilbert points out, shows a link between autoimmune disease and chemical exposures *below* levels of supposed toxicity.

To live as healthy a life as she can with lupus, Marisa Zeppieri-Caruana, 30, never takes her clothes to a dry cleaner and doesn’t use any products with pesticides. “After so many years of being sick, you learn that you *have* to be vigilant,” she says. Katie Hall looks for natural or organic beauty products. “I check everything that I put on my body because it’s just one more way chemicals can get absorbed,” she says. Erin Farley has switched from traditional cleansers to natural alternatives. “My mother taught me how to make an all- natural cleaner she calls ‘witches’ brew’: one part water, one part white vinegar and a splash of lemon,” says Farley. “I use it to wipe down everything.”

What do experts think of these steps? “I know we don’t have all the science to back it up, but I see how patients who do this are healthier and feel better, and I can only tell them that what they are doing makes sense and is a good prescription for better health,” says Dr. Mullin.

It’s a prescription Dr. Peeke follows herself. “The most important thing you can do is avoid toxic stress. Whenever you can, eat whole foods, whole foods, whole foods. And in the best of all worlds, go green,” she says. “There’s no question that if we made these kinds of changes, we would not only slow the sharp increase in autoimmune disease, we would impact heart disease, cancer and *all* health.”

Donna Jackson Nakazawa is the author of The Autoimmune Epidemic *and the website autoimmuneepidemic.com.*

http://www.glamour.com/health-fitness/2008/10/the-scariest-health-threat-youve-never-heard-of

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ABC's Robin Roberts' Sisters Participate In Breast Cancer Study

Sep 10, 2008 05:25 PM EDT

By Danielle Thomas

LONG BEACH, MS (WLOX) - Two sisters of Good Morning America anchor Robin Roberts are doing their part to fight breast cancer. You many remember how Roberts went through a very public battle with breast cancer. Now Sally Ann Roberts and Dorothy Roberts-McEwen are both taking part in the Sister Study, a research project that looks for genetic and environmental links to the disease.

Dorothy Roberts-McEwen had to be measured, poked, weighed and more to take part in the Sister Study.

"They're going to be taking information from you and asking you all kinds of questions," said McEwen. "Sometimes it can make you a little hesitant to be involved in something like that. But to me, the factors of being afraid of all that were outweighed by, 'What if something I share with this study helps other people?' So that part of it is what really inspired me to be a part of it."

McEwen is a healthcare administrator. Her sister Sally Ann Roberts is a television broadcaster in New Orleans. McEwen says their main inspiration for joining the Sister Study was their sister Robin Roberts who recently underwent treatment for breast cancer.

"Right now, the Sister Study has a really excellent representation of white American women involved in it, but it's very under-represented with women of color," said McEwen. "So there's a really big push to include our study, our information, so this study is very well balanced."

Home health practitioner Mary Jane Greenwood took McEwen's vitals for the research project. Greenwood is breast cancer survivor.

"It would be nice to be able to eradicate the disease all together," said Greenwood. "It would be nice to be able give women hope rather than fear."

McEwen said, "You can donate money and that's great. A lot of research projects need money. But to actually be a part of a research study, you don't actually get a chance to do that all the time. But if you're a sister, who has a sister who has developed breast cancer, we really encourage you to be a part of it. "

McEwen says she and her sisters have become spokespeople for the Sister Study. The trio's participation in the study will be featured in the October Issue of Essence Magazine.

If you'd like to learn more about taking part in the study, call 1-877-4-SISTER.

Medical News TODAY www.medicalnewstoday.com

Sisters Of Good Morning America's Robin Roberts Join Sister Study For Breast Cancer Research

19 Sep 2008

Sally-Ann Roberts and Dorothy Roberts McEwen LCSW, sisters of ABC's Good Morning America co-anchor Robin Roberts recently became participants and volunteer spokespersons for the Sister Study. Conducted by the National Institute of Environmental Health Sciences (NIEHS), one of the National Institutes of Health, the Sister

Study is a prospective observational study that will help researchers learn how environment and genes affect the chances of getting breast cancer. The study which is in its final phase of recruitment is committed to enrolling 50,000 diverse women who have never had breast cancer but whose sisters had the disease.

Like their sister, Sally-Ann and Dorothy are no strangers to working hard everyday to change the lives of others. Sally-Ann is co-anchor on New Orleans' CBS Eyewitness Morning News and leads a non-profit organization, Each One Save One; and Dorothy is a healthcare administrator as assistant director at South MS Regional Center. As Sister Study spokespersons, the duo will encourage more women to enroll in this important effort, which researchers hope will identify causes of breast cancer and yield information that will help prevent breast cancer for generations to come.

Breast cancer hit close to home when their younger sister, Robin was diagnosed in 2007. It was natural for them to be strong for one another through Robin's recovery but they were less accustomed to sometimes feeling helpless as they watched their sister battle the disease. Sally-Ann, 54, and Dorothy, 51, both decided that enrolling in the Sister Study would be a way to honor Robin, contribute to a good cause and hopefully help scientists learn about the causes of the disease.

"I learned about the Sister Study while interviewing another study spokesperson on the show," said Sally-Ann. "I immediately felt that this was an opportunity for me to help answer questions about why Robin may have gotten breast cancer while I had not." She added, "Future generations will truly benefit from the collective efforts of sisters participating in this study." While on air, Sally-Ann promised to join the Sister Study and did in fact honor that promise.

The news segment not only encouraged women of New Orleans to enroll, increasing local enrollment by 29%, but Sally-Ann's commitment motivated her younger sister Dorothy to enroll and also become a spokesperson. As a social worker Dorothy understands the need for research, but wasn't sure about participating herself. But, like other women who hear about the Sister Study, she overcame her initial reluctance to participate.

"When I compared the amount of time it takes to participate in the Sister Study to the countless hours my sister Robin spent fighting breast cancer, I got past my hesitation and signed up," said Dorothy. "It's so important to develop solutions that will answer questions about the environment, genes and breast cancer." She added, "Unless a wide range of women take their place in research helping to answer these questions, being able to prevent this disease in the future becomes nearly impossible. Sally-Ann and I are encouraging more women to participate, and make a difference in the fight against breast cancer."

Sally-Ann and Dorothy will tell their stories and reach out to women in their communities and beyond. The three sisters will also be featured in the October issue of *Essence Magazine.*

Fewer than 20% of women with breast cancer have any family history of the disease, and less than half of all women diagnosed with breast cancer have any of the known risk factors. Sister Study researchers believe there is much more to be learned about how environment and genes are related to breast cancer

risk. Sisters of women with breast cancer have about twice the risk of developing breast cancer themselves, as compared to most women so studying these sisters may provide important clues to breast cancer causes. Important clues will also come from studies that include a wide range of women from different backgrounds which is why the researchers are so committed to enrolling a diverse cohort.

Women ages 35 to 74 may be eligible to join the study if they have never had breast cancer themselves; their sister (living or deceased) related to them by blood, had breast cancer; and they live in the United States or Puerto Rico. The study is quickly approaching the goal of enrolling 50,000 diverse women, but to ensure the results benefit all women, researchers are asking African Americans, Latinas, Asians, Pacific Islanders and Native Americans to enroll immediately. Caucasian women with a high school degree or less, or who are between the ages of 65-74 are also still needed.

The study is no longer enrolling new volunteers who are Caucasians 35-64 years old with more than a high school degree - these women are already well represented in the study group. During the remaining months of enrollment, the Sister Study is making special outreach to women who have ever held blue collar or non-traditional jobs, because of the wide-range of environmental and chemical exposures that might be found at work.

Dale Sandler, Ph.D., Chief of the Epidemiology Branch at NIEHS and Principal Investigator of the Sister Study said, "After four years, we are almost at our goal of 50,000 participants and the team is working extremely hard to wrap up recruitment during these last few months of 2008." She added, "Over time, we look forward to continuing to follow the participants and having results that could benefit our daughters and granddaughters."

Sister Study partners include NIH's National Center on Minority Health and Health Disparities, the American Cancer Society, Sisters Network Inc., Susan G. Komen for the Cure, Breast Cancer Network of Strength, and the Intercultural Cancer Council. In addition to working with its national partners, the Sister Study works with local, regional, and national organizations to inform diverse women about the study.

To volunteer or learn more about the Sister Study, visit http://www.sisterstudy.org, (for Spanish http://www.estudiodehermanas.org), or call toll free 1-877-4SISTER (877-474-7837). Deaf/Hard of Hearing call 1-866-TTY-4SIS (866-889-4747). All activities are available in English and Spanish.

http://www.medicalnewstoday.com/articles/122060.php

Cell-Based Assay News
September 12, 2008

NTP Hosts RFI Meeting to Develop 'Rigorous, Comprehensive' HTS Toxicity-Screen Battery

By Charlotte LoBuono

Research Triangle Park, NC — The National Toxicology Program, seeking information on how to identify and select critical cellular toxicity pathways to be interrogated by cell-based high-throughput screens, this week held a Request for Information meeting at its facility here, and said it will use the responses to develop what it terms a "rigorous and comprehensive" battery of high-throughput assays, an NTP official told *CBA News*.

The NTP also solicited recommendations on particular molecular targets within these cell-tox pathways that are most informative for profiling the pathways in both cell-based and biochemical assays, and on technologies and assay systems that may enable a comprehensive approach to high-throughput toxicological screening.

"The simplest reason for [the meeting] is that we are interested in identifying both critical pathways and assays that inform on those pathways, that provide information relevant to those pathways," Raymond Tice, acting chief of the National Toxicology Program biomolecular screening branch, told *CBA News* in an interview following the first day of the meeting.

Researchers are evaluating chemicals and their relationship to toxicity through their own experiences and their methodologies, Tice said. He explained that companies employ people with experience in a particular arena, who then start thinking about how to apply their experience and expertise from drug-discovery and toxicology perspectives.

"So, by having a meeting, we start bringing together a critical mass of people," and all of those people who are in the NTP Toxicology in the 21st Century focus group on pathways and assays get all this information, see the presentations, think about it, and then go back to those companies that they feel have the most interesting approaches and do a follow-up, Tice explained.

"I think that not only was this meeting of benefit to those of us in the government as we develop these screening approaches as alternatives to investigating toxicology, but I think it also was of benefit to the participants" because it brought people together from all over the country who may have similar interests but who may not have communicated with each other before, said Kristine Witt, a toxicologist at the NTP biomolecular screening branch.

Witt told *CBA News* that "one of the things that I was pleased to see was how much discussion occurred among the attendees during the breaks and during lunch." Because many pharmaceutical companies are currently reorganizing their businesses and laying off research staffers, this is a good time for cell-based assay tool and technology companies to consider diversifying beyond drug discovery into areas such as toxicology, said John Westwick, president and CEO of Odyssey Thera and a presenter at the meeting. Westwick told *CBA News* that the meeting could be a prelude to something bigger, such as an RFA.

"It is also nice to have some external validation for what you are doing," he said. Toxicology strategies are likely to be similar to drug discovery, which Westwick said seems to spark the question, "'Is the line being blurred between environmental and pharmacological toxicology, allowing companies to expand into both spheres?'"

Interagency Collaboration

In February, the National Human Genome Research Institute and the National Institute of Environmental Sciences signed an agreement with the US Environmental Protection Agency to use the NHGRI'S National Chemical Genomics Center high-speed automated screening robots to test suspected toxic compounds using cells and isolated molecular targets (see *CBA News*, 2/15/08).

Witt said this week that the NTP is looking for assays that are ready to be installed as soon as possible, or could be installed shortly following modification, at the NCGC screening program.

"[H]earing about the options at this meeting will allow us to think about how we might develop that full, comprehensive screening program."

In addition, "As our program grows, it is going to expand, and we have to look at other options that go beyond the capabilities of NCGC, because they are exploiting a particular technology, and there are limits to that technology," Witt said.

As the NTP examines the significance of the biological responses that it comes across in the NCGC's high-throughput screens, "we will have to move into different kinds of systems, so hearing about the options at this meeting will allow us to think about how we might develop that full, comprehensive screening program," Witt said.

The NCGC will ultimately have a library of about 8,000 to 10,000 compounds, comprising "every single chemical that we can find that is of environmental concern or in commerce, or is of interest to organizations such as the EPA, NIEHS, or the US Centers for Disease Control," said Tice.

These compounds generally have to be those about whose structure something is known. They should also purchasable and should be soluble in DMSO because that is the vehicle in which the center tests its compounds. "There are certain limits to the kinds of compounds in the library, but there will be a library that gets tested," said Tice.

The NCGC also has limits in terms of the assays it runs in that they have to be a compatible with a 1,536-well format and be add-on assays. Within that context, however, the NCGS has the ability to test large numbers of compounds.

The EPA's ToxCast program, another part of the memorandum of understanding signed between the EPA, NHGRI, and the NIEHS, focuses on contracts with small companies, each of which has a spectrum of assays.

"What we are trying to do is take the data from the NCGC, which involves screening lots of compounds, but fewer assays, with that from ToxCast, which involves many assays but fewer compounds, and integrate it with the data that we already have from animals, and human data that we are trying to get from the FDA — whatever we can find," said Tice.

There is probably built-in redundancy in those assays. For example, different companies measure estrogen receptor activation in different ways. "By looking at the redundancy, we will be able to look at the total package and determine if the data is consistent for a particular compound and across different assays measuring different or related endpoints," Tice said.

Companies, organizations, or individuals in the scientific community are joining ToxCast who are not being paid by contract, but who are testing ToxCast's 320 phase 1 compounds anyway in their own assay systems, to leverage what they are trying to do.

"We are trying to … bring these companies and individuals in who may test the same compounds on their own dime to further their own efforts," Tice said.

In terms of follow-ups to the RFI meeting, "one of the questions that we are still trying to resolve is, "'How do you prioritize pathways?'" said Tice. That may be a practical issue, in terms of there may be an assay for that pathway that already can be put into high throughput.

However, another pathway may exist that is more valuable from the standpoint of disease, but for which an assay has not been developed. "What we will do is put out RFPs that say we are interested in having someone develop assays using an SBIR grant in that particular pathway or arena," said Tice.

In addition to Odyssey Thera, shops that play in the cell-based assay market that participated in the RFI meeting included Invitrogen, PerkinElmer, Promega, BioSeek, DiscoveRx, and Cellumen.

"We did not have any criteria" for inviting companies to participate," Tice said. "These are companies that actually submitted something to us and said that they were interested in attending. To the best of my knowledge, we did not turn anyone down."

http://www.cba-news.com/issues/5_36/features/149368-1.html

HealthNews

Deep Pockets Being Opened for Parkinson's Research

By: Lara Endreszl
Monday, 22 September 2008

Parkinson's disease (PD) has affected the global awareness by striking people within the public eye that we look up to and can empathize with. In 2003 I saw Pope John Paul II in an audience at the Vatican and under the weight of Parkinson's, the leader of the Catholic Church had no power against the will of his own body; his hands shook instead of waved, his body was hunched over in pain, and his voice trembled with instability. Stung like a bee with the diagnosis in 1984, Mohammed Ali, an honored man and boxing legend, is now confined to a wheelchair and while he still attends functions as a living sports legacy, he nods and twitches his head and hands not to the words being spoken or the songs being sung but to the beat of the Parkinson's resounding in his head; he hasn't won this fight yet. Michael J. Fox, a beloved character for years from television to the future on the big screen and back again, is most often recognized now as the brave young actor who was diagnosed at age 30 and is still fighting against the disease's crippling effects. With the exposure of Parkinson's disease reaching high-calibers, it's no wonder that The National Institute of Environmental Health Sciences (NIEHS)—a division of The National Institutes of Health (NIH)—is reaching deep into their pockets. It looks like the global awareness of the PD has sparked an interest in the reasons behind the diagnoses and what we can do to find a cure.

Over the next five years, NIEHS will grant $21.25 million to three research schools in the United States to fund studies relating to how environmental factors contribute to the cause, prevention, and treatment of Parkinson's disease. A central nervous system disorder, Parkinson's disease affects over one million Americans each year and the disease progresses with age. In most cases, scientists don't know specifically what brings on the disease, but some cases are known to be caused by severe head trauma (such is the speculation in Mohammed Ali's case) or patterns of genetic abnormalities. Parkinson's is thought to be a derivative of genetic mutations and outside environmental causes. For example, prolonged exposure to pesticides is thought to double a person's risk for the disease.

The three grantees are from respected research schools around the country and are using their grants to cover a specific area of researching the disease. Gary Miller, Ph.D., at Emory University, Atlanta, Georgia, receives a grant for prolonged research of how environmental and genetic factors change dopamine cells within the brain that lead to Parkinson's disease. The second grant goes to Marie-Françoise Chesselet, M.D., Ph.D., at the University of California, Los Angeles, who plans to specifically research pesticides that may be the main cause of sporadic Parkinson's diagnoses and possibly come up with a prevention plan by cautioning the use of certain pesticides. Lastly, Stuart Lipton, M.D., Ph.D., Burnham Institute for Medical Research in La Jolla, California, will investigate free radical stress caused by environmental toxins that cause genetic mutations responsible for helping to progress the disease and hopefully be able to isolate the body's proteins damaged in the process.

Acting director of the Division of Extramural Research and Training at NIEHS, Dennis Lang, Ph.D., said of the grantees, "The UCLA and Emory CNS grants will extend the exciting lines of research previously supported by NIEHS, while the Burnham Institute grant will bring an important new perspective to research on gene-environment interplay in Parkinson's disease."

Perhaps the most influential person in my life who lived with Parkinson's disease wasn't a public figure and wasn't world-renown for anything special; she was my grandmother. She raised seven children in a modest home, she was a do-gooder and revered by the community for her cooking talent and quilting techniques. As the years rolled by and she wasn't able to stand up much less get out of the house, my dad's mother spent her remaining years cooped up in a nursing home shaking and drooling, but always believed that she would walk again. That faith was finally lost in April 2005 when—the same day as Pope John Paul II—my grandmother passed on. With the generous research grants from NIEHS dedicated to finding a cure, I hope continuing investigations will be able to finally give those living with Parkinson's the second chance at life they deserve.

http://www.healthnews.com/medical-updates/deep-pockets-being-opened-parkinsons-research-1818.html

The Chronicle of Higher Education

Hidden Hazards: Could pollutants trigger Alzheimer's and Parkinson's diseases?

By Lila Guterman

Dec. 9, 2008

The symptoms of Alzheimer's or Parkinson's diseases are frightening: They include memory loss, change of personality, gait disturbance, and speech problems.

Worse is the caprice with which the diseases appear to choose their sufferers. Seemingly healthy people gradually become completely unlike themselves. Although scientists have discovered genes that increase the risks of both diseases, the genes account for just a small percentage of the millions of cases.

And so researchers are searching the environment for a cause, or causes, of neurodegenerative disease. They have theorized that exposure to pesticides or metals may trigger neuron loss or damage, perhaps decades before symptoms begin. These diseases that primarily affect the aged may even begin in the womb.

But figuring out which exposures matter is extraordinarily difficult. Such sleuthing can be tricky for any human disease — in looking backward at a person's life history, the best scientists can do is to identify likely causes.

When it comes to neurodegenerative disease, the link to toxins is even harder to establish. A person's exposure to a pollutant is usually not measured or recorded. Remembering an episode some 60 years earlier is difficult under the best of circumstances, and even harder when memory is affected by Alzheimer's disease.

But thanks in part to some lucky breaks, researchers have been making progress in studies of large human populations and in experiments on animals. They have shown that early exposure to low levels of pollutants can end up killing neurons in the same areas of the brain that are damaged in people with neurodegenerative disease. In some cases, people known to have inhaled or ingested the same pollutants have proved more likely to experience dementia or motion disorders.

The payoff of such research could be more than just a stronger grasp of which chemicals to avoid. The diseases have proved difficult to understand, and no drugs exist that stop their progression. Working out how various compounds induce the diseases in animals could help scientists better understand their mechanism in people.

To aid such research, the National Institutes of Health announced in September that it had awarded $21-million in grants to scientists who study environmental causes of Parkinson's disease. "It's very important to have a lifetime perspective," says Giancarlo Logroscino, a professor of neurology at the University of Bari, in Italy. "Even if these are diseases of aging, what happens in early life can be important."

Although something besides genetics must explain all or even most cases of Parkinson's and Alzheimer's diseases, the evidence of environmental risk factors is much stronger for Parkinson's.

Scientists have long looked for similarities among sufferers of Parkinson's. Epidemiologists typically study people who have the disease and compare their life histories with those of healthy counterparts. Such studies have turned up risk factors like living on a farm or drinking well water, and being exposed to certain metals.

But other studies have looked at the same characteristics and found no link to disease. That's a difficulty with epidemiology: Unless the exposure causes huge changes in health, connections can be hard to

ferret out. Perhaps the studies that find no link just involve too few people. Or perhaps the studies that do find connections are statistical flukes.

The key is to keep looking in different populations. "The evidence as it accumulates is getting stronger," says Freya Kamel, a research scientist at the National Institute of Environmental Health Sciences, in North Carolina.

Researchers agree that smoking, surprisingly, offers some protection against Parkinson's disease. And, says Kamel, the weight of the evidence shows that pesticides increase the risk of the disease.

A question that remains, though, is which pesticides? Most studies track exposure to pesticides only as a group instead of looking at specific herbicides, insecticides, or fungicides. Many of these pesticides can no longer be detected in the body years after exposure; some are gone after only weeks or months.

But research in this area got an unexpected boost in 1982 after seven drug users in Northern California showed up at emergency rooms displaying symptoms of Parkinson's disease. A neurologist from Stanford University, J. William Langston, discovered that they all had used a batch of heroin contaminated with a compound called MPTP.

Fingering MPTP as the responsible agent took a lot of medical detective work. "I remember thinking that if the medical director of the hospital knew how much time I was spending on a single case, he would probably fire me," Langston says.

Langston, who is now scientific director and chief executive of a nonprofit organization he founded, the Parkinson's Institute and Clinical Center, recalls the moment when he realized MPTP was the culprit. "Just like an explorer who hits a new land and knows there will be a rush of people behind him," he says, "I stood there for a moment and enjoyed the view."

The day that his results appeared in Science, his phone rang off the hook. Every researcher calling asked the same question: Where can I get MPTP? The company that made it had sold out immediately.

Quickly, scientists discovered that MPTP could cause Parkinsonian symptoms in monkeys. (The compound thus provided scientists with their first experimental version of the disease.) In the body, MPTP converts to a molecule called MPP+ and systematically assaults neurons in the same area of the brain that is damaged in Parkinson's patients.

The benefits to science of the chance discovery were tremendous. Researchers now possessed strong evidence that a chemical in the environment could cause Parkinson's disease.

The MPTP case is science's only "clear-cut demonstration," Logroscino says, that a specific toxin can induce a chronic disease of any type. (Even though lung cancer, for example, has been clearly linked to cigarette smoking, scientists do not know what elements of the smoke are to blame.) The molecule itself, MPP+, pointed directly at a pesticide as a potential bad actor. The chemical structure of MPP+ is remarkably similar to that of paraquat, a widely used herbicide, suggesting that the product might wreak havoc in the same way in the brain.

Studies in animals have since shown that paraquat kills neurons, but its effects on mouse brains do not perfectly mirror the attack by Parkinson's disease on human brains. A spokesman for the company that sells paraquat, Syngenta, calls the relevance of mouse data for human health "dubious." A controversy among scientists continues about the relevance of paraquat experiments to Parkinson's disease — it was debated this year in the pages of Toxicological Studies and discussed in October at the annual International Neurotoxicology Conference.

Acting alone, paraquat may not cause changes resembling Parkinson's disease. But Deborah A. Cory-Slechta, a professor of environmental medicine at the University of Rochester, discovered in the late 1990s that when mice received shots of both paraquat and a fungicide called maneb, their brains started

to look much more like those of Parkinson's patients. Neurons died only in the area of the brain that was damaged in Parkinson's disease.

"Never when we started this did I think we would see the kinds of things we actually saw," Cory-Slechta says. The two pesticides acted in synergy on the brain.

Cory-Slechta's team later discovered that if they gave mice shots of the pesticides very early in life, the neurons that produced dopamine gradually died off throughout the rodents' lifetimes. (Dopamine is the neurotransmitter that runs low in the brains of Parkinson's patients.) If they then exposed those mice again as adults, the effects were stronger than after the first exposure even though no traces remained of pesticide from that first dose. That showed that the toxicity to the brain was cumulative.

Cory-Slechta does not yet understand the synergy or the delayed effects, and guesses that there may be many other pairs of chemicals that could also act together. "It's frightening when you think about it," she says. "How many of these things are going on that we don't know about?"

Philip J. Landrigan, a professor of pediatrics and of community and preventive medicine at Mount Sinai School of Medicine, calls Cory-Slechta's results "tantalizing."

A group of researchers including Kamel and Langston is also making use of human data to try to blame or exonerate individual pesticides. In the mid-1990s, the National Institutes of Health began a study of workers in North Carolina and Iowa who apply pesticides, including checkups and surveys every two years about the workers' pesticide use. Nearly 80,000 people participate.

"It's a huge gold mine," Langston says. The researchers are writing manuscripts now and expect to publish results soon. Langston says their results should be "somewhat definitive."

But Landrigan argues that, to real-ly connect cause with effect, studies need to measure peoples' exposure to chemicals from birth — or even from the womb — till death. The National Children's Study, an enormous endeavor to study the health of 100,000 children, is scheduled to begin in the coming months. It plans to follow the children until they are 21, but, says Landrigan, "I'm sure 21 years from now people aren't going to just walk away."

Science will not wait decades for such studies to take place. And so it continues with animal research, which has recently produced intriguing links between Alzheimer's disease and chemicals in the environment.

Richard M. LoPachin, a professor of anesthesiology at Albert Einstein College of Medicine, has found that a class of chemicals called type-2 alkenes can damage neurons in rats in a way similar to harm seen in the brains of patients with Alzheimer's disease. The chemicals are common environmental pollutants that are heavily used in manufacturing, agriculture, and other industries.

What's more, other researchers have found that the brains of patients actually produce the same types of chemicals. He proposes in an article published this fall in NeuroToxicology that external exposure to the pollutants may work together with the internally produced compounds to speed Alzheimer's disease toward its sad conclusion.

No one has looked in human studies for links between those alkenes and neurodegenerative diseases. "It's a brand new idea," says LoPachin. "We're waiting for epidemiology to catch up to it."

Meanwhile, another contaminant may also set people up for the dread disease. Nasser H. Zawia, a professor of toxicology at the University of Rhode Island, published research in 2005 that found that baby mice fed small quantities of lead — that already-worrisome pollutant — produced, as adults, the proteins that are one of the signatures of Alzheimer's disease.

Mice do not develop plaques in their brains, as people do, so it was not clear how well their brains resembled the brains of people with Alzheimer's disease. But Zawia got lucky: He found a group of monkeys that had been born in 1980 and fed, by a scientist, with infant formula containing lead. The elderly monkeys lived at the National Institutes of Health until 2003, when scientists euthanized them and stored tissues from various organs, including their brains.

"It was a miracle to find them," Zawia says.

In January, Zawia wrote in the Journal of Neuroscience that, remarkably, no traces of lead appeared, but the monkeys' brains were full of plaques.

"Everybody thought lead was just a problem for children," Zawia says. So researchers had not done experiments with older animals that had been exposed to lead early in life, as his mice and monkeys had. Scientists usually have neither the patience nor the money to do those longer experiments, he says. He hopes to study whether people who were exposed as small children to lead are more likely to get Alzheimer's disease.

He and other scientists emphasize that although the environmental hazards' links to brain disease are unexpected and frightening, they are not reason to panic. Most peoples' exposure to the pollutants is very low, and the diseases are complex and most likely require more than one instance of bad genetic or environmental luck.

"I don't talk about [pesticides] as causing Parkinson's disease," says Cory-Slechta. "I think of these as risk factors."

Zawia agrees. If you were exposed to lead as an infant, he says, you may have "the deck stacked against you. But that does not mean you will get Alzheimer's disease."

http://chronicle.com/weekly/v55/i16/16b01001.htm

THE UNIVERSITY OF ARIZONA® UA News

Binational Enviromental Outreach and Education Efforts Honored

UA researchers are invited to speak at National Institute of Environmental Health Sciences Hispanic Heritage event.

By Rebecca Ruiz-McGill, University Communications
September 23, 2008

The National Institute of Environmental Health Sciences has invited University of Arizona researchers Denise Moreno and Monica Ramirez to speak about their educational outreach to the Hispanic community.

The National Institute of Environmental Health Services, also known as NIEHS, provides federal research funding to universities for environmental health and science research projects.

Moreno and Ramirez are program coordinators for both the NIEHS Hazardous Waste Program and the U.S.-Mexico Binational Center for Environmental Sciences and Toxicology housed within the UA's College of Pharmacy. The Hazardous Waste Program conducts studies concerning hazardous environmental contaminants along the border region.

The Binational Center supports environmental science and toxicology training, research and policy development. In association with these two projects, Moreno and Ramirez conduct community outreach with a special focus on Spanish-speaking communities.

"The funding from NIEHS involves faculty members, staff and students from 5 UA colleges and 10 departments who are applying their expertise to hazardous waste issues," Ramirez said. "It is an interdisciplinary approach to environmental research and education with a central theme in detecting, assessing and ameliorating environmental pollution and determining the impact of environmental pollution on human health."

Their presentation will include discussion of their outreach efforts, including the training of community health advocates or promotoras, who advise businesses on how to minimize pollution, as well as conserve energy and water. They also will share their work on making hazardous mine tailings safer and will also discuss the development of a youth science program, which was offered in the summer of 2008 to students living along the Arizona-Mexico border.

"The program works to translate years of study into real world solutions and moves science projects and research from the laboratory to the field," Moreno added.

The NIEHS Diversity Council selected to feature Moreno and Ramirez's work as part of its 2008 Hispanic Heritage Celebration.

http://uanews.org/node/21627

The New York Sun

Founding Dean Named for CUNY School of Public Health

By E.B. Solomont, Staff Reporter of the Sun
September 29, 2008

A former top official at the National Institutes of Health, Dr. Kenneth Olden, has been appointed founding and acting dean of the proposed CUNY School of Public Health at Hunter College.

Previously, Dr. Olden headed the National Institute of Environmental Health Sciences and the National Toxicology Program, both parts of the NIH. He recently served as Yerby Visiting Professor at the Harvard School of Public Health.

"Dr. Olden is a distinguished scientific leader and cancer researcher," CUNY's chancellor, Matthew Goldstein, said in a statement announcing the appointment. "He brings an impressive combination of national and indeed international experience and service to the country to this vitally important and new initiative."

Plans for a school of public health were announced in October 2006. Billed as the city's first public school of public health, it plans to offer master's and doctoral degrees. It is expected to open by 2010.

http://www.nysun.com/health-fitness/founding-dean-named-for-cuny-school-of-public/86780/

curetoday.com

Chemical Reactions

By Laura Beil

December 24, 2008

We live our lives in the company of chemicals, from the pollution that makes its way into our air and food, to the synthetic material in the products we use every day. These compounds are considered safe, based on tests that look for the degree of exposure necessary to trigger DNA damage. But just as epigenetics is changing the way people think about cancer, it's starting to change the way people think about cancer causes.

"I think the field of epigenetics is going to turn the field of toxicology on its head," says Randy Jirtle, PhD, of Duke University Medical Center. Why? Because it raises the possibility that low levels of chemicals—chemicals now considered safe—are in fact silently marking our DNA in ways that can lead to cancer.

And these pollutants might not only affect our lives, but our children and grandchildren. In 2006, scientists from Washington State University reported that mice exposed to a certain fungicide experienced epigenetic changes that were passed to future generations. Preliminary data have suggested similar connections with smoking.

At this point, little is certain, says Jirtle, who has conducted experiments with bisphenol A, a controversial chemical found in plastic bottles and canned-food liners. Experiments on bisphenol A have suggested that the compound, which is so ubiquitous it can be measured in the bodies of 93 percent of Americans, can cause epigenetic changes. But the research has been conducted in laboratory rodents, and animal epigenomes differ from humans. This is the case for most chemicals: Data on the epigenetic impact is either non-existent or limited to laboratory experiments.

The federal government is now trying to change that, with the National Institute of Environmental Health Sciences (part of the National Institutes of Health) investing almost $30 million in epigenetic studies of environmental exposures over five years. Some of the first human data from those studies may be released soon, says Fred Tyson, PhD, a scientific program director at NIEHS. The pollutants under examination include arsenic, air particulates, bio-active dietary zeranol (from injected cattle), dietary biotin, polychlorinated biphenyls (PCBs), and polycyclic aromatic hydrocarbons (byproducts of burning fossil fuels).

"It's possible it (epigenetics) could have some policy implications for what acceptable levels of exposure are," Tyson says, though no one can yet say what the outcome of the research will be.

Jirtle believes that, at the very least, the most common environmental pollutants need to be reexamined for safety. "It's been assumed that since they don't cause mutations that they aren't problematic," he says. "I don't think that's good enough."

http://www.curetoday.com/index.cfm/fuseaction/article.showArticleByTumorType/id/98/tumorCategory/Myelodysplastic%20syndrome/article_id/951

SELF
HEALTH

Cancer in a can?

There's mounting concern that a chemical in the lining of food cans and in some plastic containers may cause health problems. Here's how to protect yourself.

By Bijal Trivedi
From the October 2008 Issue

When she first hung up with her doctor one December day in 2004, Rachael Rawlins could only cry. "I was shocked, surprised, incredulous," she says. The doctor, who had biopsied two lumps in her breast, informed her that she had aggressive cancer and needed a mastectomy. Later during her chemotherapy, Rawlins, an environmental lawyer in Austin, Texas, did what she does best: She searched for answers. "I was only 40. It wasn't in my family. I was very fit. I didn't drink much alcohol. I didn't think I had any risk factors." Rawlins wondered if she'd been exposed to a toxin that could have had anything to do with the cancer. She and her husband began trawling the Internet for leads.

What she found was compelling: bisphenol A (BPA), a harmless-seeming material that is an ingredient in certain plastics. It is used to line billions of cans and in other forms of packaging, including polycarbonate water bottles, those hard, shatterproof containers often used for sports. Rawlins learned that in ultra-low doses—the amount that can leach from packaging and bottles into food and drink—BPA has been shown in lab animals to cause immune disorders and early onset of puberty, and to fuel various cancers.

Most every drop of Rawlins's drinking water had contact with BPA, she says. The cooler at her office, where she drank the most, was likely made of BPA. At home, she stored filtered water in a polycarbonate container from Whole Foods and was especially careful when she was pregnant. "While I was trying to protect myself and my babies from pollutants, the entire time the water was being contaminated by its container," she says.

CHEMICAL INACTION

In the past year, the dangers of polycarbonate baby and water bottles have gotten a lot of press. Not so BPA levels in food, which is how most Americans are exposed to the substance, according to the Centers for Disease Control and Prevention in Atlanta. If BPA affected Rawlins's cancer, some of her exposure may also have come from her food.

Food cans are lined with epoxy resins made up of approximately 60 percent BPA, which prevents the cans from rusting and the contents from picking up a metallic taste. But minute amounts of BPA, which are not chemically bound in the resin, seep into food and beverages. What's more, BPA is also sometimes present in pizza boxes made from recycled materials, as some of the paper they're made from contains BPA. The American Chemistry Council in Arlington, Virginia, which represents BPA manufacturers, and the Food and Drug Administration insist that the amounts from packaging that wind up in food are harmless. Last year, the Environmental Working Group (EWG) in Washington, D.C., tested 97 canned items from three states for BPA. They looked at beans, fruit, liquid meal replacements, infant formula, pasta and soup and found that 57 percent of the foods were contaminated—although with amounts well below what the Environmental Protection Agency says is safe.

DOSE AND DANGER

The EWG finding sounds like good news, but many experts say it's not—what are thought to be safe levels may still pose a threat to a fetus or child, and to adults as well. Some say there's no such thing as a safe dose. In fact, most people are already exposed to amounts that cause alarming effects in animals, says Retha Newbold, Ph.D., head of developmental endocrinology at the National Institute of Environmental Health Sciences in Research Triangle Park, North Carolina. Nearly 93 percent of Americans have BPA in their urine, according to the CDC study. Although Newbold says the amounts in our blood are some 250-fold lower than the dose the EPA considers safe, she is not reassured: "We do not have definitive proof that these low doses cause adverse effects in humans—but I don't know if we want to wait for definitive proof."

Most people agree that BPA is harmful in large quantities. As it has done with many high-volume industrial chemicals, the EPA has conducted standard risk-assessment studies. In 1982, toxicologists exposed adult rats to high doses of BPA in order to identify the largest dose that proved harmless and extrapolated what they thought would then be a safe dose for humans. The EPA then divided this dose by 1,000 to protect more vulnerable citizens and account for any undiscovered risks. The final "safe" dose is 50 micrograms per kilogram of body weight per day. This standard was confirmed in 1993 and holds today. When rats are exposed to more, their body weight begins to drop. In mice, very high levels will kill the mother and her fetus.

But what is dividing scientists, industry types and regulators is whether trace amounts of BPA—parts per billion, 0.0000000705 ounces—that leach from packaging might, in fact, pose a different kind of danger than a high dose. In traditional toxicology, the basic scientific principle is the higher the dose of a poison, the greater the effect. But if the substance is a hormone—and BPA is structurally similar to estrogen—things work differently: Low doses may also produce a great effect, although of a different kind. "That's not intuitively obvious," says Newbold, who studies how estrogen and estrogenlike chemicals affect the genes. So similar to estrogen is BPA, that, like an evil twin, it mimics the hormone by fulfilling some of its duties—interacting with proteins and DNA in a way that only estrogen should. Recent studies on animals have shown that BPA can switch on and off genes that would normally be under the hormone's control.

CANCER CONNECTION

Ordinarily, estrogen is present in small quantities for brief periods while a fetus (human or animal) is developing, and that is enough to lay the foundation for the reproductive system and the architecture of milk ducts and lobe tissue in the breasts. After this, estrogen is mostly absent until puberty onward, when cyclical secretion of estrogen stimulates the turnover of healthy cells to keep them in working order. One of estrogen's main functions is to make breast cells multiply. Every time this happens, a cell is vulnerable to carcinogens and DNA mutations. That's why over a lifetime, the risk of breast cancer increases naturally: The more estrogen a woman is exposed to, the greater the risk.

But getting too much estrogen during fetal development—whether naturally or in the form of a man-made endocrine disrupter such as BPA—creates abnormally developed breast tissue in the fetus that grows into adult tissue that is unusually sensitive to estrogen.

Animal studies clearly show these effects. Maricel V. Maffini, Ph.D., research endocrinologist at Tufts University School of Medicine in Boston, exposed pregnant mice to extremely low doses of BPA. Then she studied the development of the offsprings' mammary glands. Those whose mothers took in even minuscule amounts had accelerated breast development. "Everything is hyperactive," Maffini says. In a similar study, rats exposed in utero were examined at four months—the equivalent of a woman in her early 20s—and their breasts showed precancerous cells and tumors. "The mammary gland is like a network of pipes all going to the nipple," Maffini

explains. "When cells lining the pipe grow inward, the pipe gets blocked." That cluster of abnormal cells is the first stage of tumor formation, and a third of the BPA-treated animals had blockages. None of the untreated ones did. In short, BPA seemed to prime the fetal rats for cancer, so when they were exposed to natural estrogen as adults, the abnormally developed tissue overreacted and proliferated into cancerous tumors.

Newbold's experiments bring home the idea that even fleeting exposure to BPA can trigger cancer later in life. She exposed mice to minute doses for the first five days of their life. At 18 months, she found that the mice suffered from a significantly greater number of uterine tumors and fibroids, and ovarian cysts than the unexposed animals. Some increase in the incidence of tumors is normal with aging, but these tumors arose earlier, at about 12 months (equivalent of age 40), in mice exposed to BPA, and there were more of them. "That seems to match what we are seeing in the general population," of humans, Newbold says: More women being diagnosed younger and with more aggressive tumors.

As scientists learn more about the effects of low doses of BPA, a series of disturbing health trends begins to make sense. BPA has been used in cans and plastics since the 1950s, and there has been a rise in prostate and breast cancers in Europe and the United States since that time. Initial studies with human cells do little to calm fears. Shanaz H. Dairkee, Ph.D., senior scientist for cancer research at the California Pacific Medical Center Research Institute in San Francisco, exposed noncancerous breast cells in women with breast cancer to a "safe" dose of BPA. She then compared the gene activity in these cells with typical gene activity in breast cancer cells. Although BPA did not transform normal cells into cancer cells per se, it did have a Jekyll and Hyde effect: BPA caused groups of genes in healthy cells to behave abnormally, as they might in the aggressive cancer cells. "This shows cause and effect," Dairkee says.

That's not to say that BPA is the sole or primary trigger of breast cancer. "I think that BPA, along with a number of environmental estrogens, is playing a role in the increase in incidence in a number of cancers. I don't believe it's BPA alone," Newbold says. Dairkee says a woman's genetic makeup plays a larger role. "For some people, BPA may have no effect." But if a woman is prone to cancer or has an early stage of it, "then exposure to BPA may lead to a more aggressive form that is almost impossible to cure," she says.

WHAT'S BEING DONE

A draft of a government report, which was expected to be finalized in late summer, does not capture the urgency that Newbold and others think it should. The National Toxicology Program of the National Institute of Environmental Health Sciences has "some concern" that low doses of BPA could alter mammary and prostate development in fetuses, and that females could experience early puberty. But it has "negligible" concern that these levels pose a danger to pregnant women.

Although Canada has proposed banning the sale of baby bottles containing BPA and many retailers and manufacturers such as Toys "R" Us, Wal-Mart and Nalgene are phasing it out, little is being done about food packaging. The Environmental Working Group study of canned goods found that, depending on the type of food, a mere one to three servings could expose a woman or child to the doses of BPA that caused serious adverse effects in animals. "We have all the pieces of the puzzle," says Anila Jacob, M.D., who worked on the EWG study. "A good start would be to ban its use in all food packaging." In June, Massachusetts congressman Edward J. Markey proposed exactly that. "For the sake of the health of every man, woman and child in America, the best course of action we can take right now is to completely ban BPA in food and beverage containers, especially because there are alternatives already available."

For now, a ban seems unlikely. BPA is heavily produced—between 6 and 7 billion pounds each year, says John Peterson Myers, Ph.D., chief scientist of Environmental Health Sciences, a not-for-profit science education organization in Charlottesville, Virginia. "So there's a lot of money at stake," Myers says.

Banning the chemical, even in children's products, as has been proposed in California, is unnecessary, industry representatives say. "There is only limited and inconclusive evidence from laboratory animals. Additional research is needed to see whether these findings are relevant for human health," says Steven G. Hentges, executive director of the Polycarbonate/BPA Global Group at the American Chemistry Council. "Science supports the safety of BPA." The FDA concurs that BPA is safe for use in baby and children's products and in food packaging. "Dietary exposure to BPA from these uses...is well below the levels that would cause adverse health effects," Norris Alderson, Ph.D., associate commissioner for science at the FDA, testified before Congress in May.

"It is mind-boggling that regulators and industry can still ignore the low-dose studies," Myers contends. He says that if the government acknowledged that testing high doses of chemicals may not predict the effects of low doses, it would be forced to look more closely at hundreds of other endocrine-disrupting contaminants. "The system doesn't protect public health," Myers says. "It protects products."

Proving that Rachael Rawlins's cancer was connected to BPA is impossible. Because everyone in the United States is continually exposed to BPA, there is no control group with which to compare the rates of cancer. Still, for Rawlins, the BPA ban was immediate. She and her husband "tossed all plastic, because we weren't sure which things contained BPA," she says. They now use glass and stainless steel. She also eschews canned foods and eats mostly organic products.

Rawlins, who is now healthy, has become a grassroots advocate, talking to friends, neighborhood associations and retailers about BPA. When she comes across people using polycarbonate bottles, she'll "give them my five-minute speech" on the chemical and the controversy. She's also writing law and policy articles and trying to get the government to regulate BPA and other toxins more tightly. "I am not a scientist," she says. "But I don't need proof that BPA harmed me. It is enough that the studies indicate there is a serious risk of harm. If I had been informed, I would not have taken that risk."

http://www.self.com/health/2008/09/cancer-from-food-packaging?currentPage=2

SELF
HEALTH

Steering clear of BPA

If you'd like to avoid bisphenol A, as environmental biologist Retha Newbold advises women with a family history of cancer or those of childbearing age to do, try these tips.

By Bijal Trivedi
From the October 2008 Issue

Sip from stainless steel of glass, which do not contain BPA. Some plastics do and it's not easy to tell which ones. If you use plastic, avoid any with 7 in the recycling triangle on the bottom. These codes were never meant to indicate the presence of BPA and so are not foolproof guides, but numbers 1 through 6 are less likely to contain the chemical.

Nuke food in ceramic or glass. High temperatures make BPA in plastic containers more likely to leach. Avoid putting plastics (polycarbonate especially) in the dishwasher.

Stick to fresh or frozen foods. Most cans are lined with BPA-epoxy liner. Of foods tested, the highest levels of BPA were in pasta, vegetables and soups. But many haven't been tested.

Demand BPA-free cans, as advocate John Peterson Myers advises. Eden Foods in Michigan uses BPA-free cans for all low-acid foods. They cannot be used for acidic items such as tomatoes, however, so stick to glass jars for foods like that.

http://www.self.com/health/2008/09/how-to-avoid-bisphenol-a?

The Times-Tribune.com

Wide range of opponents lining up to contest route of 500,000-volt PPL line

First in a two-part series

By David Singleton, Staff Writer

Monday, October 6, 2008 10:27 AM EDT

When a pair of administrative law judges recommended in August that the state Public Utility Commission reject a proposed high-voltage transmission line in southwestern Pennsylvania, Peter Derrenbacher found the news encouraging.

But he finally allowed himself to hope two weeks ago after prospective builder Allegheny Energy Inc. bowed to public opposition and announced it will seriously scale down the proposed $1.1 billion project in Greene and Washington counties.

Mr. Derrenbacher, president of the Saw Creek Estates Community Association in Pike County, knows the proposed Susquehanna-Roseland Power Line is a different project by a different utility in a different part of the state.

But in what he characterizes as a David-versus-Goliath struggle to keep PPL Electric Utilities from putting its 500,000-volt transmission line through the heart of their 3,000-home development, residents will take inspiration wherever they find it.

“It shows that when these proposals are made by these utilities, they are not irreversible,” Mr. Derrenbacher said. “What is implied is going to happen may not necessarily happen.”

The swift unraveling of the Allegheny Energy project, known as the Trans-Allegheny Interstate Line, or TrAIL, provides an intriguing backdrop against which PPL will make the case for its line.

PPL expects to ask the PUC by year’s end for authorization to construct the 99-mile line from the Susquehanna nuclear plant in Luzerne County’s Salem Twp. to the Delaware River near Bushkill. That’s where it will meet a similar line Public Service Electric and Gas Co. wants to build between the river and its Roseland substation in New Jersey.

PPL spokesman Paul Wirth insists the TrAIL case will not change how the Allentown utility approaches the Susquehanna-Roseland project.

Jeff Schmidt, state director of the Sierra Club, thinks the western Pennsylvania case is going to be almost impossible for the utility to ignore.

“We see that decision as an important foundation upon which the PPL power line proposal will have to be debated,” he said.

State Consumer Advocate Irwin A. “Sonny” Popowsky, whose office intends to intervene in the PPL case, just as it did on the TrAIL application to the PUC, cautioned against reading too much into the outcome in western Pennsylvania.

“One thing I can say is, each line has to be judged on its own merits,” Mr. Popowsky said.

Battle brewing

PPL’s application to state regulators will set in motion a review process in which the company and other

formal parties, such as the PUC's Office of Trial Staff, the Office of Consumer Advocate, environmental groups and individuals, will present evidence to an administrative law judge.

Consumers who don't wish to file a formal protest can still make informal complaints to the PUC. In addition, the administrative law judge will conduct public input hearings separate from the formal evidentiary hearings.

After reviewing the evidence and arguments, the administrative law judge will recommend a decision to the PUC. The commission may accept, reject or modify the decision.

Transmission line siting reviews typically involve two questions: Is the project needed? Is the proposed route the best of the alternatives, given factors such as safety and environmental impacts?

PPL will argue the Susquehanna-Roseland line is necessary to prevent overloads on 23 transmission lines in Pennsylvania and New Jersey as early as 2013.

The recommended route, one of three alternatives considered, follows the path of an existing 230,000-volt transmission line — acknowledged by the utility as the primary reason for its selection.

In the TrAIL case, Allegheny Energy proposed construction of a 37-mile, 500,000-volt line from Washington County through Greene County to address local reliability issues. It would have been part of a larger, 240-mile high-voltage line extending through West Virginia and Virginia to the Washington, D.C., area.

But the two administrative law judges who handled the case concluded the local line wasn't needed, branding it "a grandiose answer to a minor or nonexistent problem." They also found the utility failed to make a case for the interstate line, saying the "true impetus" was to transport cheaper, coal-generated electricity to mid-Atlantic markets.

In addition, the judges hit the utility on route selection, saying its siting decisions were mandated by pre-existing right-of-way agreements, and said its proposal failed to adequately address the potential impacts on public health and safety.

On Sept. 22, faced with the unfavorable recommendation and continuing public outcry, Allegheny Energy scrapped plans for 36 miles of the proposed power line. Instead, under a proposed settlement with Greene County officials, it would build a 1.2-mile, 500-kilovolt line to link a new substation in southern Greene County to the remainder of the line at the West Virginia border.

EMFs sure to be debated

One of the health issues in the western Pennsylvania case is almost certain to be an issue when PPL takes its project before the PUC — exposure to electromagnetic fields.

Electromagnetic fields, or EMFs, are unseen lines of force associated with the transmission and use of electricity. Because of the ubiquitous nature of electric power, people are constantly being exposed to electric and magnetic fields of varying strength, produced by everything from power lines to auto ignitions to electric razors.

But since the late 1970s, when studies first suggested an association between long-term exposure to magnetic fields and the incidence of childhood leukemia, EMFs have become an elusive bogeyman in the debate over where to site — and not to site — high-voltage lines.

As the judges in the TrAIL case noted in their decision, "No issue in a proceeding to locate and construct high-voltage transmission lines is more controversial or fraught with more conflicting information than the alleged effect of exposure to electromagnetic fields."

The PUC has no formal position on EMFs, spokeswoman Jennifer Kocher said. Mr. Popowsky said to the extent a utility can take steps to minimize public exposure to EMFs at a “modest and reasonable” cost, his office will push those.

Linda Erdreich, Ph.D., a New York epidemiologist and health risk assessment specialist who has been working with PPL as a consultant, acknowledged associations between EMFs and childhood cancer have been observed.

But there is inadequate evidence to show a cause-and-effect relationship between long-term EMF exposure and any disease, despite repeated attempts to find it, she said.

Still, she understands why EMFs are such a hot-button issue in power line discussions.

“There is nothing — nothing — more important to people than their children,” Dr. Erdreich said. “Childhood leukemia is scary ... no matter how weak the evidence is.”

Christopher Portier, Ph.D., associate director of the National Institute of Environmental Health Sciences, said while there is no definitive evidence magnetic fields cause childhood leukemia, the association between the two is clear.

What is still unclear is the mechanism behind the association, whether it is the field or something else, Dr. Portier said.

The link is strong enough that both his agency and the World Health Organization classify EMFs as a possible human carcinogen.

“There is an association,” he said. “You can’t minimize the association by wishing it away.”

Louis Slesin, editor of Microwave News, a respected online journal that has covered EMF-related issues for more than 25 years, said a favored argument of utilities is magnetic fields from appliances such as hair dryers and can openers are often stronger than those directly beneath power lines.

The logic, Mr. Slesin said, is spurious. While fields from appliances are high, they drop off “really, really quickly” at distance, much more quickly than the field from a 500,000-volt transmission line, he said. And while you can choose not to use a hair dryer, there is often no option if a utility decides to put a line near your house.

“Your exposure is 24/7,” Mr. Slesin. “That’s the issue. It is the chronic exposure.”

PPL looks to mitigate EMFs

PPL is planning to take steps to minimize exposure to EMFs generated by the new transmission line in accordance with a magnetic field management program it put in place in 1991 for new or rebuilt lines, Mr. Wirth, the utility’s spokesman, said.

The benefit of a couple of those is self-evident; as Mr. Slesin says when it comes to EMFs, “Distance is your friend.”

Instead of the 85-foot towers that now carry a 230,000-volt line along most of the route, the towers PPL will construct for the new line will be 175 to 185 feet tall. And although the utility already has the easements in place in most cases, the right of way beneath the line will expand from 150 feet to 200 feet.

But Mr. Slesin said the easiest way to get rid of a magnetic field is through phasing, or arranging the lines in such a way to cancel out or reduce the field. According to PPL, phasing can reduce the strength of a magnetic field by up to 69 percent.

Mr. Wirth said PPL plans to use a technique known as reverse phasing, employed in the configuration of the double-circuit transmission lines, along the entire 49-mile length of the line from the Peckville area to the Delaware River.

That is the span that runs past the homes in Saw Creek Estates. Mr. Wirth said PPL models show EMF levels in the development will be lower after the 500-kilovolt line is in place than they are now with the existing 230-kilovolt line.

There may be portions of the line where a different phasing arrangement produces lower EMF readings, such as the 13-mile stretch in the Scranton area where the new line will parallel the existing 230-kilovolt line, Mr. Wirth said.

“The bottom line is that we will use the phasing arrangement that produces the lowest EMF readings,” he said.

‘100 percent adverse impact’

Rocco Pannozzo, vice president of the Saw Creek Estates Community Association, said whether it is the EMFs, the unsightly transmission towers, the impact of construction on the environment, or any combination of those, the PPL project has no positives for people who live along the route.

“There is going to be a 100 percent adverse impact — period,” he said.

Like many of his neighbors, Mr. Pannozzo believes the utility is motivated by greed, viewing the line as a conduit to sell more power to Northeast markets.

“The question that comes up is, where is the real need for this?” he said. “Is there really a justifiable need for this line to begin with?”

Mr. Popowsky, the consumer advocate, expects that question to be the central issue when PPL takes the Susquehanna-Roseland proposal to the Public Utility Commission. If nothing else, the TrAIL case in western Pennsylvania demonstrated the project will not be rubber-stamped, he said.

“What people can take from that,” Mr. Popowsky said, “is the Pennsylvania Public Utility Commission will give careful consideration to not just what the company has to say but what the residents and customers in Northeastern Pennsylvania have to say.”

http://www.thetimes-tribune.com/articles/2008/10/06/news/sc_times_trib.20081006.a.pg1.tt06powerline_s1.1982018_top2.txt

toledoblade.com

October 6, 2008

Sister study focuses on genetic link to cancer

Research to include varying backgrounds

By Julie M. McKinnon
Blade Staff Writer

Moore

Ruge

Gerber

Marilyn Moore was more worried about her twin sister going through treatment for breast cancer than her own ordeal with cervical cancer about a year earlier.

So when Ms. Moore heard about the Sister Study Breast Cancer Research project - which is focused on looking at environmental and genetic causes of the disease - she knew without asking that two of the twins' sisters would join her in volunteering for the 10-year effort.

The natives of rural Attica, Ohio, hope to help researchers looking for causes of breast cancer in women like Carolyn Ruge of Toledo, their 53-year-old sister who was successfully treated two years ago.

Yet Ms. Moore, Ms. Ruge's twin, said she has tried with no avail to recruit others to the study conducted by the National Institute of Environmental Sciences, one of the National Institutes of Health.

"I don't know why they would be hesitant," Ms. Moore of Shelby, Ohio, said. "To me, it is a no-brainer. Why wouldn't they want to do it?"

Scientists are in their final push to get the last of 50,000 participants for the study, which three of Ms. Ruge's sisters joined two years ago. Minority women aged 35 to 74, including those of African, Latina, and Asian descent, are especially in demand to make the study representative of American women.

So far, 2,023 women from Ohio and 2,179 from Michigan have volunteered for the study, and all participants are eager to help, Lisa DeRoo, the study's lead investigator, said.

"They're very much invested in the study," she said. "A lot of them are doing it in memory of their sisters or in honor, if they're a survivor."

Ms. Moore and another sister participating in the study, Denise Gerber, 48, of Bellevue, Ohio, said they worry about whether they or other relatives could get breast cancer. The family's four brothers and five sisters, including study participant Darlene Hart, 54, of Richmond, Ind., collectively have 12 daughters and 11 granddaughters so far.

"You are concerned about them, because no one wants to put their children at risk," said Ms. Ruge, mother of Jessica Lashley of Toledo, 30, and grandmother of Olivia Lashley, 6.

Added the breast cancer survivor: "There has to be some link."

Having a sister with breast cancer doubles a woman's risk to have breast cancer, which could be because of genetics or shared environmental exposures, said Ms. DeRoo, the scientist from the National Institute of Environmental Sciences. Some special analysis likely will be done on twins such as Ms. Moore and Ms. Ruge, she said.

Participants start with telephone interviews and questionnaires, and they provide samples of their blood, urine, nails, and household dust so scientists can assess various factors and exposures believed to cause cancer, including arsenic and other chemicals, Ms. DeRoo said. Most of the study's work is done up front, she said.

Ms. Gerber, Ms. Ruge's sister in Bellevue, said they were all weighed and measured, and they were asked to recall living conditions from childhood.

"You had to really go back," she said.

Participants answer a questionnaire annually for 10 years to update their medical conditions, but they do not take medication or otherwise alter their lifestyle, Ms. DeRoo said.

"They're just supposed to do what they normally do," she said.

http://www.toledoblade.com/apps/pbcs.dll/article?Date=20081006&Category=NEWS32&ArtNo=810060318&SectionCat=&Template=printart

THE NEWS&OBSERVER
newsobserver.com

Oct 07, 2008

Telecommuters look smart as gas prices go up

Bruce Siceloff, Staff Writer

Gloria Jahnke wants to have it both ways. And who doesn't?

Most days, she wants to rub elbows with her stimulating colleagues at the National Institute for Environmental Health Sciences.

"I like that interaction," said Jahnke, 60, a health scientist in toxicology. "You run into people during the day. You learn things you wouldn't pick up otherwise."

But sometimes -- no disrespect to those brainy NIEHS types -- Jahnke just wants to shut out all distractions. She needs to sit at her computer and stay focused on her deadline.

On those days, she can get more work done at her house in Orange County. After all, she has a phone at home, a laptop and an Internet connection.

So why waste time and gas on a 45-minute drive to Research Triangle Park? This summer, Jahnke joined the ranks of a modest movement to let workers stay home a few days a month -- and phone it in.

Telecommuting isn't new, but it seems to be growing. As $4 gas makes driving more expensive, some bosses are getting up the courage to let workers out of their sight every now and then.

Cisco Systems, with 4,500 full-timers in RTP, ranked sixth this year in Fortune magazine's survey of the 100 best places to work -- partly on the strength of its No.1 rank in telecommuting. About 70 percent of Cisco employees work from home at least one day a week.

When 12,210 Triangle-area commuters pledged in the SmartCommute Challenge this summer to try a different way of traveling to work, 5,806 of them said they would telecommute.

A national nonprofit group that promotes commuter benefits cited NIEHS recently for a 33 percent increase this year in what the federal agency calls teleworking.

Jahnke is among 113 of the 950 employees at NIEHS who occasionally work from home. She started work there in May and got approval this summer to try telecommuting one day every other week. So far, she likes it.

"I like having that option when you have to focus," said Jahnke (pronounced Yon-kee). "You don't want an interruption. Nobody can actually pop in to see you unless they drive out there to your house. That can help, if you really have to get things done."

Márcia Clover of Apex says her 2-year-old at home is less a distraction than co-workers at her office. She works for Clean Design, an RTP advertising agency.

When she was preparing for her daughter's birth two years ago, she agreed to take a reduced pay raise if her bosses would let her work at home two days a week.

Good gas savings

"Then when gas prices started going up, I was like, man, that was a good choice," said Clover, 34. "The two days I save on gas and day-care costs make a difference at the end of the month."

Clover's work on advertising projects includes interactive programming, video editing and writing. She can do all that, and even log her daily work hours, on her home computer.

Each Wednesday and Friday, she skips the 30-minute drive to RTP and starts work early.

"I feel like I'm more productive the days I work from home -- even with a 2-year-old -- than when I'm at the office," Clover said. "She's really good. I take a five-minute break every now and then to read a book to her."

Because she keeps her files at home, bad weather doesn't keep her from doing her job.

"My productivity, rain or shine, it's still the same," Clover said.

NIEHS began moving a few years ago to protect itself against natural and manmade disasters that might interrupt work at its RTP campus. Suddenly, working at home was government policy.

"So when management bought into it, that really changed things," said Dick Sloane, who promotes commuter alternatives as part of his job at NIEHS. "We have a number of managers who telework, and they're strongly enthusiastic."

Some government agencies are still catching up.

The state Department of Transportation is leading a quiet effort to help state workers cut back on their driving. DOT and other agency workers are eligible for vanpool subsidies, free bus rides and flexible work hours.

But in 2003, DOT managers canceled a program in which more than 100 employees were allowed to work from home a few days a month. Five years later, DOT still does not allow telecommuting.

http://www.newsobserver.com/news/story/1245631.html

PLUS A DESPERATE DAD GIVES UP HIS NINE KIDS

OCTOBER 20, 2008

People

NICOLE RICHIE

MY LIFE AS A MOM

Nine months after baby Harlow's arrival, Nicole and Joel talk about loving parenthood. 'I can't imagine life without her,' says Joel

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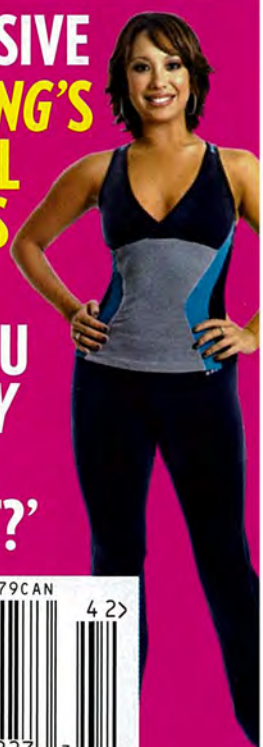

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BREAST CANCER SURVIVOR
ROBIN ROBERTS AND HER SISTERS

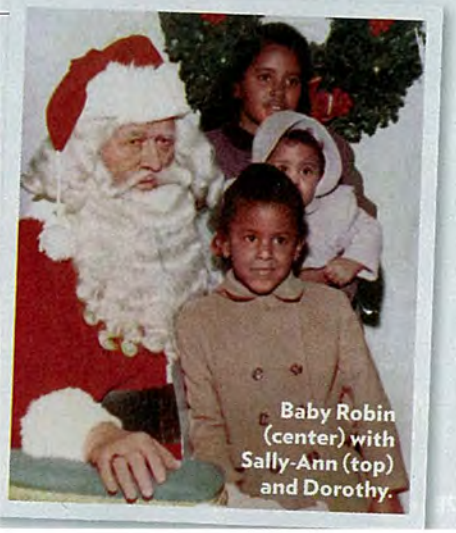
"They've carried a load for me," says Roberts (at home in New York City with Sally-Ann, left, and Dorothy).

The Power of Three

Her cancer was aggressive and could recur at any time. But with sisters Sally-Ann and Dorothy on her team, the *Good Morning America* coanchor says nothing can stop her

The night before her breast cancer surgery last August, Robin Roberts roamed around her New York City apartment, too scared to feel anything. "I was in a fog," she recalls. But the *Good Morning America* coanchor wasn't alone. Her 84-year-old mother, Lucimarian, was there and so were her big sisters: Sally-Ann, who'd flown from Louisiana, air mattress in tow, and Dorothy Roberts McEwen, up from Mississippi. At one point, Robin placed Dorothy's hand on her own right breast so Dorothy could feel the malignant mass. Dorothy's eyes widened in shock. "It was like marble, like a rock," she recalls. "I thought, 'Oh, my God.'"

It was a momentary lapse. For the most part Dorothy, 52, a healthcare administrator, and Sally-Ann, 55, a New Orleans news anchor, have been towers of strength for their baby sister, visiting and phoning through the entire roiling journey, from the discovery of Roberts's cancer in the summer of 2007 to



Baby Robin (center) with Sally-Ann (top) and Dorothy.

Photograph by AMY ARBUS

> "Yes, I am living with cancer. But don't go 'woe is me.' I don't want it. Don't need it" –ROBIN ROBERTS

her emotional on-air announcement, partial mastectomy, chemotherapy and radiation. The siblings have also helped by enrolling in the Sister Study, a National Institutes of Environmental Health Sciences survey of women whose sisters have suffered from breast cancer [see box]. "I have good days and bad days," says Roberts, 47, amply energetic as she bantered with her sisters at home Sept. 27. "I'm dealing with the side effects [from chemo]. I get sinus infections and colds. I walk like an old lady in the morning and evening."

"People I don't know write to say, 'I'm getting my mammogram,'" says Roberts (modeling at a Fashion Week show in February).

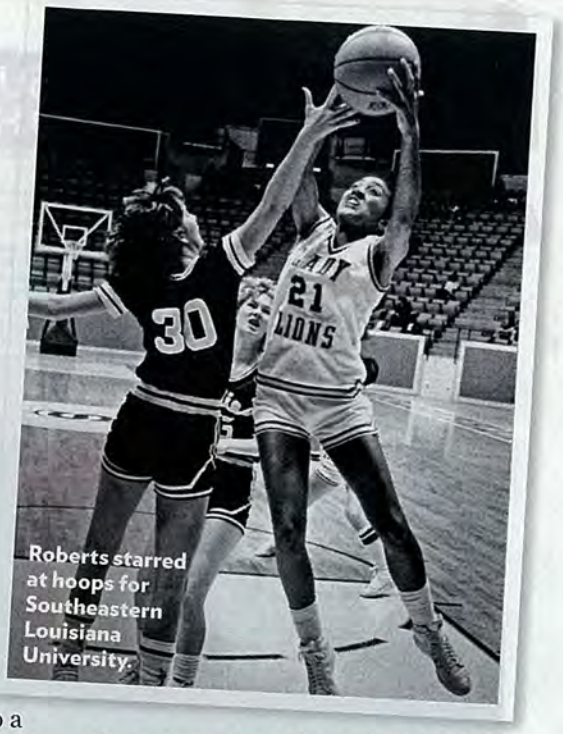
Growing up in the small town of Pass Christian, Miss., the Roberts girls (who have a brother Lawrence, 60) were always close. Sally-Ann recalls Robin as a good-natured pleaser. "I'd say 'Go into the house and bring the Oreos' and she would.'" The dynamic would change. As Roberts grew up into a success as a local sports reporter, making the leap to ESPN and *GMA*, she "became the leader, the organizer, the benefactor," Dorothy says. But after her diagnosis, Roberts admits, "I felt like the baby again."

Tears stream down her face as she recalls an especially grueling round of chemotherapy. "I was in bed, and had this terrible sore on my leg," she says. "Sally-Ann said, 'What's that?' I said that's the chemo trying to get out of my body. She just put her hand on my leg and started praying." Then there was the time Dorothy made her a butterfly bracelet that said, "You're my breast friend." Says Robin: "It's those sweet, unspoken things."

The sisters flew north again last December after Roberts, depressed near the end of her chemo, asked for them. "I knew she really needed us," Dorothy says. "She'd be on TV smiling, but when I saw her in her apartment, she was like, 'I had a good life. If I don't wake up tomorrow, I'm okay.'"

After three weeks off and some long walks with KJ, her Jack Russell, Roberts rebounded. She remains resolutely positive, though acutely aware that a recurrence could lurk in the shadows. "I'm not telling you I'm cancer-free," she says. "I have a very aggressive type called triple-negative that happens in a lot of African-American women. I had a screening last week, and nothing showed up. The trick is to find it early." Aside from doctor's visits every couple of months, she undergoes acupuncture, sees a nutritionist and hits the gym. "Yes, I am living with cancer," she says. "But don't go 'woe is me.' I don't want it. Don't need it. I'm still in the game. I don't want to say 'survivor.' I want to thrive."

By Sharon Cotliar and **Richard Jerome**



Roberts starred at hoops for Southeastern Louisiana University.

FROM LEFT: DIANE BONDAREFF/AP/SOUTHEASTERN LOUISIANA UNIVERSITY

THE SISTER STUDY

African-American women are less likely than white women to develop breast cancer but slightly more likely to die from it. One reason, experts say, is they are prone to the aggressive "triple-negative" variety (in which tumors resist some targeted treatments). The NIEHS is recruiting more women of color to the Sister Study (sisterstudy.org), designed to analyze genetic and environmental risk factors over a life span among some 50,000 women. To begin with, those enrolled offer samples of blood, urine and toenails as well as household dust. They also answer yearly medical questionnaires. Says study director Dr. Dale Sandler: "We hope to get some answers."

The New York Times
nytimes.com

Dentists Back Sealants, Despite Concerns

By Tara Parker-Pope
October 21, 2008

Cavities or chemicals? That's the dilemma for parents worried about a controversial substance found in the popular sealants that are painted on children's molars to prevent decay.

The chemical is bisphenol-A, or BPA, which is widely used in the making of the hard, clear plastic called polycarbonate, and is also found in the linings of food and soft-drink cans. Most human exposure to the chemical clearly comes from the food supply. But traces have also been found in dental sealants.

Although the Food and Drug Administration has reassured consumers that the chemical appears to be safe, it has received increasing scrutiny in recent months from health officials in the United States and Canada.

The National Toxicology Program, part of the Department of Health and Human Services, has raised concerns about BPA, particularly over childhood exposure to the traces that leach from polycarbonate baby bottles and the linings of infant formula cans. The 2003-4 National Health and Nutrition Examination Survey by the Centers for Disease Control and Prevention found detectable levels of BPA in 93 percent of urine samples collected from more than 2,500 adults and children over 6.

BPA has estrogenlike effects, and animal studies have suggested that exposure may accelerate puberty and raise a potential risk of cancer. This month, the journal Environmental Health Perspectives reported that the chemical might interfere with chemotherapy treatment. And last month The Journal of the American Medical Association reported that adults with higher levels of BPA in their urine were more likely to have heart disease or diabetes.

Despite these concerns, the American Dental Association remains strongly in favor of sealants. Dentists note that numerous studies show that any exposure they cause is negligible and temporary, lasting no more than three hours after the initial application. And other studies have found no detectable levels of BPA in most American-made sealants. Meanwhile, sealants have been shown to offer years of protection against cavities.

"This is such an enormously valuable tool to prevent tooth decay," said Dr. Leslie Seldin, a New York City dentist and consumer adviser for the American Dental Association. "The BPA issue, I think, is so minuscule in impact that it doesn't really warrant the attention it's been getting."

Dental sealants have the consistency of syrup so that they can seep into the crevices of molars. A light is used to harden the sealants, which are then buffed smooth. The coatings prevent the growth of bacteria that promote decay in the grooves of molars.

Just this month, a review of 16 studies by the Cochrane Collaboration, a nonprofit group that evaluates medical research, showed sealants offered significant protection from cavities. In the seven studies that compared sealants and regular brushing alone, the 5- to 10-year-olds who used sealants had less than half as much decay on biting surfaces four and a half years after the treatment. One study with a nine-year followup found that only 27 percent of sealed tooth surfaces had developed cavities, compared with 77 percent of unsealed surfaces.

The Cochrane review did not address BPA, but it did cite a March review article in The Journal of the Canadian Dental Association, looking at 11 major studies of BPA exposure from dental sealants. That review, financed by the nation's health system and conducted by researchers with no industry ties,

concluded that patients were not at risk for exposure to the chemical. And it noted that dentists and patients could further limit any exposure with simple steps like buffing tooth surfaces and gargling and rinsing after sealants are applied, all of which are standard practices in most dental offices.

The review also found that three products did not release detectable amounts of BPA: Helioseal from Ivoclar Vivadent; Seal-Rite from the Pulpdent Corporation; and Conseal f from SDI (North America). All carried the 2007 American Dental Association seal.

The amount of BPA exposure can vary depending on the sealant. In a 2006 article in The Journal of the American Dental Association, researchers from the United States Public Health Service and the Centers for Disease Control and Prevention studied the effects of two dental sealants on 14 men, based on saliva and urine samples. They found that patients treated with an Ivoclar Vivadent product called Helioseal F showed no change in urinary or salivary levels of BPA, while patients treated with Delton Light Cure sealant, from Dentsply Ash, were exposed to about 20 times higher doses of BPA.

Linda C. Niessen of Dentsply International said in a statement that the A.D.A. says sealants are safe, and she notes that any exposure from a sealant is “significantly lower and occurs infrequently” compared with other sources of BPA.

Parents concerned about BPA exposure should ask their dentists what type of sealants they use and whether it has been tested for BPA. But researchers from the Centers for Disease Control and Prevention offered this bottom line: “Sealants should remain a useful part of routine preventive dental practice.”

http://www.nytimes.com/2008/10/21/health/21well.html

University of Kentucky News

Two Speakers Launch Wyatt Lecture Series

Media Contact: Dan Adkins

LEXINGTON, Ky. (Oct. 29, 2008) − Two national leaders in environmental health and disease will present the University of Kentucky's inaugural John P. Wyatt Lecture at 9 a.m. Wednesday, Nov. 5, in the William T. Young Library auditorium.

William A. Suk, acting deputy director of the National Institute of Environmental Health Sciences (NIEHS) and National Toxicology Program, and Philip H. Landrigan, director of the Mount Sinai School of Medicine Children's Environmental Health Center, will be joined by three invited doctoral students.

At NIEHS, Suk assists the director in formulating and implementing plans and policies necessary to carry out the missions of NIEHS/NIH and the National Toxicology Program. He previously has served as director of the NIEHS Superfund Hazardous Substances Basic Research and Training Program and currently is director of the Center for Risk and Integrated Sciences. He has published extensively on issues linking exposures with disease and on research and prevention strategies to reduce risks of environmentally induced diseases and disorders. His presentation is titled "Environmental Exposure and Disease Links in Global Health: Addressing Health Needs and Disease Outcomes."

Landrigan, a pediatrician, epidemiologist, and internationally recognized leader in public health and preventive medicine, is a member of the Institute of Medicine of the National Academy of Sciences. He is known for his many decades of work in protecting children against environmental threats to health, most notably lead and pesticides. Landrigan served for 15 years as an epidemic intelligence service officer and medical epidemiologist at the Centers for Disease Control and Prevention and the National Institute for Occupational Safety and Health. In addition, Landrigan has been centrally involved in the medical and epidemiologic studies that followed the destruction of the World Trade Center on Sept. 11, 2001. Landrigan will speak about "Children's Health and the Environment: The Problem and the Solution."

In addition to Suk and Landrigan, UK doctoral student Zuzana Majkova and postdoctoral scholar Jignesh Pandya will speak about their own environmental health research. Also speaking about related research will be invited Michigan State University doctoral student Haitian Lu.

The event will kick off at 8:30 a.m. with a poster exhibition in the William T. Young Library Gallery.

The inaugural John P. Wyatt Lecture is made possible through the Dr. John P. Wyatt Endowment at UK, as well as by the UK Office of the Vice President for Research, the UK College of Agriculture, and the UK Superfund Basic Research Program.

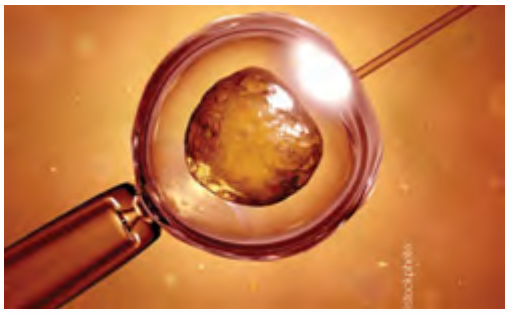
http://news.uky.edu/news/display_article.php?category=2&artid=4096

Nature Medicine
14, 1171 (2008)
doi:10.1038/nm1108-1171

As IVF becomes more common, some concerns remain

Prashant Nair, Chapel Hill, North Carolina

Introduction



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The magic moment: Fertilization of the egg

An increasing number of infertile couples have turned to assisted reproduction technology, which facilitates the union of the sperm and the egg. But, in recent years, controversial reports of birth defects in babies conceived through assisted reproduction have led a few researchers to raise concerns about the technology's safety.

Assisted reproduction includes a handful of procedures, many of which are based on *in vitro* fertilization (IVF) of the egg. In the US alone, assisted reproduction accounted for slightly more than 1% of all births in 2005, according to the country's Centers for Disease Control and Prevention. The IVF process poses some minor risks to women, including ovarian cysts, mood changes and hot flashes. But a few rare risks to the fetus have given some fertility researchers pause.

Tinkering with sex cells and embryos outside the body, scientists worry, might spur genetic changes that manifest as congenital birth defects. No direct evidence supports that notion, but epidemiological studies have shored up possible links between assisted reproduction and rare genetic syndromes in newborns, such as Beckwith-Wiedemann syndrome, a condition marked by premature birth, an enlarged tongue and heightened susceptibility to tumors, respiratory and speech defects (*Hum. Reprod. Update* **10**, 3–18; 2004).

Fortunately, the syndrome is rare: it normally affects about 1 out of every 12,000 newborns worldwide. But a study found that 3 out 65 US children afflicted with the syndrome had been conceived through IVF (*Am. J. Hum. Genet.* **72**, 156–160; 2003). In other studies, 6 out of 149 children in British and French medical registries of the syndrome were found to have been conceived through IVF or through a specialized technique called intracytoplasmic sperm injection, or ICSI (*J. Med. Genet.* **40**, 62–64; 2003; *Am. J. Hum. Genet.* **72**, 1338–1341; 2003).

"There appeared to be more children with the syndrome conceived through ART [assisted reproductive technology] than we might have expected by chance alone," says Eamonn Maher, a geneticist at the University of Birmingham, UK. Many cases of Beckwith-Wiedemann syndrome, Maher says, stem from abnormalities in DNA methylation—addition of a chemical tag called a methyl group—occurring in specific genes on chromosome 11.

Methylation is one of an array of DNA markers, called imprints, that guide normal development of the embryo. For example, imprinting seems crucial to proper brain growth, says Carmen Williams, a clinical

investigator at the US National Institute of Environmental Health Sciences in North Carolina. "The concern is that while the embryo is being cultured in the [IVF] lab, maybe the imprint marks are being changed. We know for sure that happens in mice," she adds (*Biol. Reprod.* **62**, 1526–1535; 2000).

Some studies have suggested a causal relationship between ICSI and abnormal methylation patterns (*Am. J. Hum. Genet.* **71**, 162–164; 2002; *Am. J. Hum. Genet.* **72**, 218–219; 2003). And Maher says the findings hint that imprinting defects might trigger Beckwith-Wiedemann syndrome.

But he also cautions that the absolute risk of giving birth to a child with Beckwith-Wiedemann syndrome is low.

"The disease is so rare that it's difficult to counsel an infertile couple not to go forth with ART," Williams says.

Conclusive evidence for the possible adverse effects of IVF is unavailable, owing to the dearth of long-term follow up of babies conceived through the technology. One Canadian study reported at the Society for Maternal-Fetal Medicine's conference in 2007 found that babies conceived through IVF were nearly 60% more likely to develop birth defects than naturally conceived ones. Most of the defects were gastrointestinal, although some were bone, muscle or heart related. Another study, from the University of Iowa, found birth defects in about 6.2% of about 1,500 IVF-conceived children, in contrast to 4.4% among naturally conceived ones (*Fertil. Steril.* **84**, 1308–1315; 2005).

If future studies bear out these links, Williams suggests that one can perhaps decrease the risk to the child by avoiding certain invasive procedures that might not be necessary depending on individual circumstances, such as biopsies of implanted embryos, culturing embryos in the lab longer than the minimal time period and using ICSI in the absence of male fertility problems.

http://www.nature.com/nm/journal/v14/n11/full/nm1108-1171.html

Environmental Health News

Enviro health scientists, chemists join forces to promote safe chemicals

Scientists convene in Southern California to draft a consensus statement designed to overcome obstacles to creating new, environmentally benign industrial compounds.

By Marla Cone, Editor in Chief
Environmental Health News
published 12 November 2008

In an effort to match problems with solutions, environmental health scientists and chemists convened this week to chart a path to promoting development of safe, sustainable chemicals.

Leaders in environmental health and green chemistry met at University of California, Irvine to draft a consensus statement designed to offer advice and overcome obstacles to creating new industrial compounds that won't endanger public health or the environment.

"Our understanding of toxicity has gone through a transformational evolution in the last decades. Everyday chemicals that once looked benign no longer do," said Lynn Goldman, a professor of environmental health sciences at Johns Hopkins University's Bloomberg School of Public Health.

The goal of the collaboration is to merge the knowledge and ideas of toxicologists and others who specialize in the dangers posed by chemicals with experts in green chemistry, who design nontoxic, environmentally benign materials.

Monday's session at the National Academies' Beckman Conference Center was open to the public, drawing an audience of about 200. But the scientists on Tuesday and Wednesday met behind closed doors to craft a consensus statement they plan to deliver in a few weeks to the public, particularly policymakers.

Facing scientific uncertainty, controversy generated by industry and ever-increasing complexity of issues, many environmental scientists in recent years have turned to consensus statements, which summarize the state of the science and recommend steps to address problems.

Pete Myers, chief executive officer of Environmental Health Sciences, which organized the conference with the nonprofit group Advancing Green Chemistry, said the group's mission is to avoid "yet another generation of problematic chemicals." The central theme, he said, is that new chemical compounds can be both profitable and safe.

The scientists involved in this week's meetings expressed a sense of urgency, a desire to ensure that green chemistry becomes a priority. They are particularly concerned about hundreds of industrial compounds that can disrupt hormones at low levels. Animal studies, as well as some human data, suggest that exposure to many chemicals, particularly in the womb, can alter reproduction, immune systems, brain development and other vital functions.

Endocrine disruptors are to the chemical industry what sub-prime mortgages are to the banking industry, said Terry Collins, Thomas Lord Professor of Chemistry at Carnegie Mellon University and director of its Institute for Green Science.

As with the mortgage crisis, he said, "it's important not to drag our feet."

However, many obstacles remain to promoting development of safer chemicals.

Lack of regulation, insufficient investment and inadequate training keep many chemists from embracing green chemistry. Of the estimated 83,000 chemicals in commerce, only a few hundred are "green." For the vast majority of the others, the risks are unknown.

“The current regulatory strategy of testing chemicals one by one cannot possibly identify all of the substances that threaten health,” said Joe Thornton, an associate professor in the Center for Ecology and Evolutionary Biology at the University of Oregon.

Thornton recommended three changes:

- Reform the nation’s chemical-by-chemical regulatory process.
- Put precautionary policies in place when the science about a compound is uncertain.
- End the use of chemicals with properties that are likely to disrupt hormones.

Goldman said one major barrier is that chemicals are regulated one at a time, while in human bodies, they always occur in mixtures. She said the current U.S. law, the Toxic Substances Control Act, “will never be effective unless the burden can be shifted to industry to prove a product is safe.”

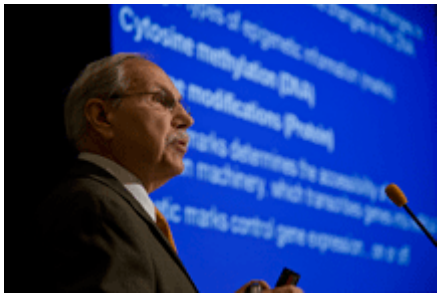
Under the law, enacted in 1976, the Environmental Protection Agency can only ban or restrict an industrial chemical if it poses an “unreasonable” risk to humans or the environment. In addition, the EPA is required to choose the “least burdensome” approach to regulate the chemicals.

As a result, the environmental agency has not banned any existing industrial chemical since 1989, when it tried to phase out asbestos. The asbestos ban was overturned in 1991 when a federal appeals court ruled that the EPA had not proven it was necessary. Since then, the agency has relied mostly on voluntary efforts by chemical companies.

The European Union already reformed its policies. Two years ago, the EU enacted the world’s most stringent law aimed at toxic chemicals, and it already is having global effects on the chemical industry, which must test and register thousands of compounds.

In September, California launched its own program, the nation’s most comprehensive reform of chemicals policy. The new law requires the state to evaluate, identify and perhaps ban industrial chemicals that are linked to health effects.

The group’s consensus statement is likely to tackle one of the newest environmental health issues--epigenetics. Some scientists believe that exposure to many chemicals can trigger heritable changes in how genes express themselves, making a person more susceptible to disease. Those changes might remain in place not just for the exposed fetus, but for all future generations.



Dr. Jerrold Heindel, NIEHS

Jerrold Heindel, scientific program administrator at the National Institute of Environmental Health Sciences, said many diseases and disorders, including asthma, obesity, attention deficit disorder and heart disease, may be triggered when fetuses, babies or young children are exposed to chemicals in plastics, cosmetics, pesticides and other consumer products.

By changing chemical policy, we can “shift the focus from curing disease to prevention and intervention," Heindel said.

When pregnant rats are exposed for a few days to a mix of two pesticides, 90% of their offspring have reduced sperm counts and 10% are infertile. And those effects lasted for at least four generations of the rats.

“If it’s true” for humans, Heindel said, “imagine the implications.” What that means, he said, is that your great-grandmother’s chemical exposure could be harming your own health and fertility.

Nevertheless, the number of students studying to become chemists is declining right at the time that innovation is desperately needed, said John Warner, president of the Warner Babcock Institute for Green Chemistry.

“The large army of practicing scientists worldwide investigating the next generation of materials has no training or skills necessary to meet these challenges,” Warner said.

Some industries are slow in following the tenets of green chemistry.

EPA officials say many high-tech industries, including the pharmaceuticals industry, are among the most wasteful in terms of the chemicals they use and the hazardous waste they create. For every kilogram of a drug they make, pharmaceutical companies use more than 100 kilograms of chlorinated compounds and other solvents that are thrown away. In comparison, the oil industry wastes a much smaller amount of solvents: 0.1 kilogram for every kilogram of product.

Many pharmaceuticals wind up in surface waters and drinking water after they are excreted. Berkeley Cue, formerly an executive at Pfizer Global Research and Development, said the biggest challenge is that a drug needs to be stable in manufacturing and in shelf life, so it is difficult to make ones that degrade to something benign in the environment.

Making environmentally benign active ingredients for drugs “is beyond our scientific understanding today,” Cue said.

Currently, drugs are screened for environmental toxicity late in the development process. Cue recommends that such screening come early in the drug discovery stage.

Chemists attending the conference said industries need incentives, sometimes regulations, to switch to environmentally benign chemicals.

Donald Blake, chair of UCI’s chemistry department who works with Nobel Laureate F. Sherwood Rowland, said the aerospace industry was resistant to eliminate metal-cleaning solvents that deplete the ozone layer. But when the Montreal Protocol phased out such substances in the 1990s, the industry discovered that a citrus-based cleaner worked just as well.

Sometimes the pursuit of profits isn’t enough to persuade companies to replace risky compounds, Warner said. For many chemicals, substitutes already have been invented, but they are not manufactured because they are big, risky investments.

Collins recommended multiple changes in policies to transform industrial chemicals, including a way to prioritize chemicals that should be replaced and elimination of all compounds that are persistent in the environment or are transported globally via the air or oceans.

“We have no choice but to embark on a course to adapt the economy to these realities,” he said.

Otherwise, chemicals invented today could harm people’s descendants hundreds of years from now.

“Trans-generational justice is really the critical thing for our civilization in the next century,” Collins said.

Link to meeting program.

http://www.environmentalhealthnews.org/ehs/news/enviro-scientists-chemists-join-forces-to-promote-safe-chemicals

THE NEWS&OBSERVER
newsobserver.com

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Looking at drugs in water

Experts gather in the Triangle to assess a public health question

Sabine Vollmer, Staff Writer

RESEARCH TRIANGLE PARK - Despite rising fear -- and rhetoric -- about the presence of pharmaceuticals in drinking water, there is actually very little evidence of whether there are health risks related to the issue.

That was one main message from 150 researchers and public health experts who huddled at the N.C. Biotechnology Center this week. The two-day conference, the first by a collaborative group of Triangle environmental health experts, was an attempt to answer some of the questions being raised by regulators, scientists and lawmakers.

Drawing on data collected by water treatment plants and federal agencies such as the U.S. Geological Survey, The Associated Press in March reported that treated drinking water in Philadelphia, northern New Jersey, San Francisco and Washington, D.C., tested positive for traces of prescription drugs, including antibiotics, mood stabilizers and sex hormones.

But more and better data is needed to figure out which pharmaceutical chemicals are likely to cause the most harm to the environment and people and how contaminants get into the water.

"We cannot afford to have the whole industry destroyed by a couple of bad actors," said Kenneth Olden, chairman of the newly formed Research Triangle Environmental Health Collaborative. The group counts the National Institute of Environmental Health Sciences, the University of North Carolina, Duke University, the U.S. Environmental Protection Agency and research institutes in the Triangle among its supporters.

"We want to provide leadership," said Olden, the former director of the NIEHS' toxicology program. "The expertise is here in North Carolina."

"There's been a lot of frustration that we've been talking about this for as long as we have and nothing is done," said Doug Finan of GlaxoSmithKline's environmental health and safety regulatory affairs.

On Tuesday, conference participants came up with several recommendations, which they plan to present to state and federal lawmakers and publish in a peer-reviewed journal:

* The EPA monitors pesticides, herbicides and other chemicals for possible harm. Researchers have long known that pharmaceutical chemicals also show up in the water, but none is on the EPA monitoring list. Lawmakers need to determine which regulatory agency should be in charge of testing water for pharmaceutical chemicals and their byproducts.

"We can't measure everything all the time," said Damian Shea of the N.C. State Department of Biology.

* Consumers need to know what to do with unused medicine. Physicians and pharmacists should be tapped as advocates to prescribe and fill only as much medicine as needed and tell consumers how to dispose properly of leftovers.

http://www.newsobserver.com/business/story/1291129.html

THE NEWS&OBSERVER
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Modified: Nov 16, 2008 05:06 AM

Some moms ditch plastic cups

Safety of additive is topic of debate

Wade Rawlins, Staff Writer Comment on this story

Conflicting reports over the safety of the plastic additive bisphenol A have forced parents to decide for themselves whether to keep using plastic baby bottles and cups made with the widely used compound.

Some, like Keira McNeill, a Knightdale mother of two, decided to stop waiting for the government to settle the safety issues. McNeill opted to replace her children's baby bottles and cups to protect them from any potential harm. Others, like Grace Danuck of Apex, still take comfort in the U.S. Food and Drug Administration's safety assessment and are taking a wait-and-see approach.

Bisphenol A, also called BPA, is used in the plastic linings of food and soda cans to prevent corrosion. It is also used in hard clear polycarbonate plastics, such as for baby bottles and water bottles.

More than 90 percent of Americans have bisphenol A in their bodies, from consuming food and beverages stored in containers made with BPA.

The FDA insists that the chemical compound is safe at low doses. But an independent science panel, convened by the FDA and including researchers from the Triangle, found in October that the FDA's safety assessment was flawed.

The advisory panel concluded the FDA should have considered a wider range of studies beyond the two industry-funded ones that found the product safe. The FDA is expected to respond to the recommendation by February.

Based on animal research, some researchers have raised questions about the chemical's effect on reproductive systems in newborns and fetuses.

In October, Canada became the first country to add bisphenol A to its list of toxic substances, because of concern that infants might be ingesting too much of the chemical, which mimics the hormone estrogen. Canada's health agency has said it would end the sale of baby bottles containing BPA and support infant formula makers in switching to different packaging. BPA leaches from plastics.

McNeill said questions raised by researchers about BPA's potential harm convinced her that her family should avoid it.

"When Canada banned it, that spoke volumes to me," said McNeill, a hospital surgical technician. "That same weekend, I went through and threw out a lot of things, all my kids' sippy cups and all the plastic dishes. To me, it should not be in things we are consuming."

But not everyone agrees. Grace Danuck said the FDA's assessment gives her a level of comfort.

"With medical science, we know so much now that we almost know too much," Danuck said. "Coffee is bad for you, then it's good for you. We can nit-pick just about anything that has less than healthy ingredients in it."

Danuck, who sells Tupperware products, said that at every housewares party, someone asks, "Is this a safe plastic?" So she did some reading to satisfy herself.

"The main thing I say to people is not everything goes in the microwave," Danuck said. "We have microwave-safe products, and within that group, some of them are polycarbonate and some are not. I feel safe with it."

The FDA has acknowledged that more research is needed on bisphenol A in light of uncertainties underscored by the advisory panel's review. The panel's report was endorsed by the FDA's science advisory board Oct. 31.

John Vandenberg, associate director for health at the U.S. Environmental Protection Agency's National Center for Environmental Assessment in Research Triangle Park, served on the review panel because of his expertise in risk assessment of chemicals found in the environment.

Vandenberg said there are a lot of uncertainties about the chemical and some hints of potential concerns. He said the FDA had not considered more narrowly focused studies that also had merit.

Vandenberg said the concern is with infants, because their bodies don't flush chemicals.

"As you age, you develop ability to metabolize or excrete chemicals differently than as newborns," he said. "Newborns don't have the same ability to metabolize."

Animal effects studied

Panel member Philip J. Bushnell, a neurotoxicologist in the EPA's National Health and Environmental Effects Research Laboratory in RTP, said some studies of bisphenol A involving animals had shown behavioral changes, suggesting gender-bending effects.

"When you have a chemical with estrogenic potency, you can change the way the fetus develops," Bushnell said. "How this translates into humans is a very big question. There is a lot more work that needs to be done to sort that out."

Michael Herndon, a spokesman for the FDA, said the panel's report raises important questions regarding the FDA's draft safety assessment and that the agency would respond by February.

The "FDA is already moving forward with planned research to address the potential low-dose effects of bisphenol A, and we will carefully evaluate the findings of these studies," Herndon said.

Kimberly Ballard of Raleigh, who has two young sons, decided to get rid of most of the plastic cups her children used.

"I would like to think our government would have our best interest at heart and our children's best interest," Ballard said. "If something comes up that could be harmful, I'd like to hear the alarms go off and someone say this is something possibly dangerous for your child."

STUDIES DIFFER ON BPA

Bisphenol A is a chemical produced in large quantities and used to produce hard clear plastics and epoxy resins. Epoxy resin is used to line metal food cans and bottle tops. The plastics are used to make products such as baby bottles and water bottles. Bisphenol A can leach out of the plastic or epoxy resin into the food or beverage.

Scientific studies offer conflicting results about the safety of bisphenol A at low doses.

After reviewing a vast number of studies, the National Toxicology Program, an interagency program that does research across the federal government, expressed "some concern" for effects on the brain, behavior, and prostate gland in fetuses, infants, and children at current human exposures to bisphenol A.

There is limited evidence of developmental changes occurring in some animal studies at doses that are experienced by humans. But it's unclear whether similar changes would occur in humans.

The FDA is not recommending that anyone discontinue using products that contain BPA. Concerned consumers should know that several alternatives to polycarbonate baby bottles exist, including glass baby bottles.

http://www.newsobserver.com/news/story/1296742.html

washingtonpost.com

ADHD Medications Don't Pose Cancer Risk

Friday, November 21, 2008

(HealthDay News) -- Two popular medications for treating attention-deficit hyperactivity disorder (ADHD) do not cause genetic damage linked to an increased risk for developing cancer, a new study says.

The study, done by researchers at Duke University Medical Center and the National Institutes of Health, counters a previous one that reported biomarkers associated with an increased cancer risk were present in the blood of children taking the ADHD drug methylphenidate.

"The new findings should help alleviate some of the concerns that were raised by the previous study," study co-author Scott Kollins, director of Duke's ADHD program, said in a university news release. "However, we need to continue to study the long-term effects of these medications and expand our analyses to include older patient populations."

The new study, which looked at methylphenidate (Ritalin LA and Concerta) and amphetamine (Adderall and Adderall XR), used a larger study sample and conditions that apply to a wider cross-section of children with ADHD than the initial study did, he said.

"We looked at three common markers associated with damaged chromosomes and did not find increased genetic abnormalities in children taking either medication, regardless of a variety of factors, such as age, sex, body weight, height, race or ADHD subtype," Kollins said.

About 2 million children have ADHD, a condition commonly characterized by inattention, hyperactivity and impulsivity. Methylphenidates and amphetamines have been used to treat the condition for decades, with millions of prescriptions written for them in the United States every year.

The study was published in the November online issue of the *Journal of the American Academy of Child & Adolescent Psychiatry*.

More information

The U.S. National Institute of Mental Health has more about ADHD.
SOURCE: Duke University Medical Center, news release, Nov. 19, 2008

(Kristine Witt study)

http://www.washingtonpost.com/wp-dyn/content/article/2008/11/21/AR2008112102135.html

REUTERS

ADHD meds do not induce cell damage

Wed Nov 26, 2008 11:48am EST

NEW YORK (Reuters Health) - Countering the findings from a 2005 study, new research supported by the United States National Institutes of Health indicates that stimulants used in the treatment of attention deficit/hyperactivity disorder (ADHD) do not cause chromosomal changes in children.

The earlier work identified an increased frequency of DNA damage and structural aberrations in chromosomes, which are associated with an increased risk of cancer. The abnormalities were observed in the white blood cells (lymphocytes) of 12 children after 3 months of methylphenidate, a drug commonly used to treat ADHD, Kristine L. Witt and associates explain in the Journal of the American Academy of Child and Adolescent Psychiatry.

Although research since then failed to replicate the earlier findings, "the enormous public health significance of this issue requires additional investigation," note Witt, at the National Institute of Environmental Health Sciences in Research Triangle Park, North Carolina, and co-investigators.

To this end, they recruited 63 previously untreated patients ages 6 to 12 diagnosed with ADHD. The children were randomly assigned to treatment with methylphenidate (Ritalin LA or Concerta) or to mixed amphetamine salts (Adderall or Adderall XR). The 3-month trial was completed by 25 and 22 subjects, respectively.

No significant treatment-related increases in cell damage were detected in the lymphocytes of the group as a whole or in the 47 subjects who were treated for the full 90 days.

According to Witt's team, these results add to the growing body of evidence that therapeutic levels of methylphenidate or mixed amphetamine salts do not induce chromosomal damage in humans.

Still, the investigators recommend that studies "continue to monitor these and related genetic damage endpoints in larger study groups...after longer exposure periods."

SOURCE: Journal of the American Academy of Child and Adolescent Psychiatry, December 2008.

http://www.reuters.com/article/healthNews/idUSTRE4AP5UL20081126

WebMD
Better information. Better health.

ADHD Drugs Don't Cause Genetic Damage

Study of Ritalin, Adderall, and Concerta Shows No Chromosomal Damage

By Salynn Boyles
WebMD Health News
Reviewed by Louise Chang, MD

Nov. 19, 2008 -- Ritalin, Adderall, and Concerta do not appear to cause genetic damage in children who take them for attention deficit hyperactivity disorder (ADHD), a new government-funded study concludes.

The findings should reassure parents concerned that the stimulant drugs used to treat ADHD may be linked to an increased risk of cancer.

Those concerns were raised by a 2005 study showing evidence of drug-related chromosomal damage in 12 out of 12 children with ADHD taking Ritalin.

The new study, conducted by researchers from the National Institutes of Health and Duke University Medical Center, shared a similar design with the earlier trial.

But it was larger and also included children taking Adderall and Concerta.

"We saw no [chromosomal] effect associated with medication in any of our treatment groups," genetic toxicologist and researcher Kristine L. Witt, MS, tells WebMD. "These findings were extremely reassuring."

ADHD Drugs and Cancer

Millions of children take either methylphenidate-based stimulants, like Ritalin and Concerta, or the mixed amphetamine stimulant Adderall for the treatment of ADHD symptoms.

Approved in 1955, Ritalin is the oldest and most widely studied ADHD drug. Adderall and Concerta have been sold in the U.S. for about a decade.

While a few animal studies have linked Ritalin use to tumor growth, the 2005 pilot study was the first human study to link Ritalin use to chromosomal damage that could promote cancer.

Subsequent studies examining the proposed link have not supported these findings.

In the current study, 47 children with ADHD between the ages of 6 and 12 took either Ritalin LA, Adderall, Adderall XR, or Concerta for three months.

Blood samples taken prior to starting the drugs and at the end of three months of treatment were assessed for chromosomal breaks, chromosome fragments suggestive of breaks, and exchanges of genetic material between pairs of identical chromosomes.

These three standard measures of chromosomal damage were the endpoints examined in the 2005 study.

But the outcomes in the two trials were very different.

"We did not see any significant treatment-related increases in any of these endpoints," Donald R. Mattison, MD, of the National Institute of Child Health and Human Development, says in a news release. "These results add to a growing body of evidence that therapeutic levels of these medications do not damage chromosomes."

Long-Term Safety of ADHD Drugs

ADHD expert Regina Bussing, MD, says the fact that the new study was publicly financed is a major strength. Bussing is a professor of psychiatry at the University of Florida, Gainesville.

"This was a high-quality study that was funded by the government, not the drug industry," she says.

Duke University ADHD program director Scott H. Kollins, PhD, who also participated in the study, says it is now clear that ADHD drugs do not cause chromosomal damage. But he adds that important questions remain about their long-term safety.

"We don't have a lot of information about long-term effects," he tells WebMD. "We need to follow patients on these drugs to address other concerns."

Concerns about the impact of long-term stimulant use on growth and later-life substance abuse have yet to be addressed, he says.

There are also suggestions that years of stimulant use during childhood might increase the risk for heart attacks and strokes during adulthood.

"We still don't know if treating a child for 15 years with these drugs will have a long-term impact on hypertension or other cardiovascular risk factors," he says. "We have no evidence that it will, but these studies have not been done."

SOURCES:

Witt, K.L. Journal of the American Academy of Child & Adolescent Psychiatry, December 2008; vol 47: pp 1375-1383.

Kristine L. Witt, MS, genetic toxicologist, National Institute of Environmental Health Sciences, Research Triangle Park, N.C.

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Donald Mattison, MD, senior advisor to the director, National Institute of Child Health and Human Development.

Regina Bussing, MD, professor of psychiatry, University of Florida, Gainesville.

http://www.webmd.com/add-adhd/news/20081119/adhd-drugs-dont-cause-genetic-damage

UPI.com

ADHD drugs don't cause genetic damage

Published: Nov. 20, 2008 at 8:33 PM

BETHESDA, Md., Nov. 20 (UPI) -- Two common medications used to treat attention-deficit hyperactivity disorder do not appear to cause genetic damage in children, U.S. researchers said.

Research at the National Institutes of Health and Duke University Medical Center in Durham, N.C., provides new evidence that therapeutic doses of stimulant medications, such as methylphenidate and amphetamine, do not cause cytogenetic, or chromosomal, damage in humans.

The study, published in the Journal of the American Academy of Child and Adolescent Psychiatry, looked at three measures of cytogenetic damage in white blood cells of each child participating in the study, and found no evidence of any changes after three months of continuous treatment.

"This is good news for parents," said study co-author Kristine L. Witt, a genetic toxicologist at the National Institute of Environmental Health Sciences. "Our results indicate that methylphenidate- and amphetamine-based products do not induce cytogenetic damage in children."

However, the researchers emphasize that the findings should not be interpreted as final proof of the long-term safety of stimulant drugs for the treatment of ADHD.

"More research and close monitoring of children taking these medications for extended periods of time is needed to fully evaluate the physical and behavioral effects of prolonged treatment with stimulants," study co-author Scott H. Kollins of Duke University said.

http://www.upi.com/Health_News/2008/11/20/ADHD_drugs_dont_cause_genetic_damage/UPI-29911227231234/

consumeraffairs.com
knowledge is power!

ADHD Meds Seen as Safe for Kids

New research refutes fears that medicines cause genetic damage

November 21, 2008

In contrast to recent findings, two of the most common medications used to treat attention deficit hyperactivity disorder do not appear to cause genetic damage in children who take them as prescribed, according to a new study by researchers at the National Institutes of Health and Duke University Medical Center.

The study published online this month in the Journal of the American Academy of Child and Adolescent Psychiatry (JAACAP) provides new evidence that therapeutic doses of stimulant medications, such as methylphenidate and amphetamine, do not cause chromosomal damage in humans.

The researchers looked at three measures of cytogenetic damage in white blood cells of each child participating in the study and found no evidence of any changes after three months of continuous treatment.

"This is good news for parents," said Kristine L. Witt, M.Sc., a genetic toxicologist at the National Institute of Environmental Health Sciences and co-author on the study. "Our results indicate that methylphenidate- and amphetamine-based products do not induce cytogenetic damage in children."

The researchers involved emphasize that the findings should not be interpreted as final proof of the long-term safety of stimulant drugs for the treatment of ADHD.

"More research and close monitoring of children taking these medications for extended periods of time is needed to fully evaluate the physical and behavioral effects of prolonged treatment with stimulants," noted Scott H. Kollins, Ph.D., director of the Duke ADHD Program and a co-author of the paper.

ADHD is a disorder characterized by attention problems, impulsivity, and hyperactivity. About 3 to 5 percent of children in the United States have been diagnosed with the disorder, although several studies suggest 7 to 12 percent of children may be affected.

http://www.consumeraffairs.com/news04/2008/11/adhd_kids.html

REUTERS

Fibroid growth differs in black and white women

Last Updated: 2008-12-01 17:00:53 -0400 (Reuters Health)

NEW YORK (Reuters Health) - Differences in the growth of fibroid tumors may explain why black women typically have more symptoms than white women, according to a study in the Proceedings of the National Academy of Sciences.

Fibroids, also known as leiomyomata, are growths within the walls of the uterus. Although almost always benign, these tumors can become quite large and produce heavy menstrual periods, pelvic pain, and other symptoms. They occur in about 25 percent of all women and are the leading cause of hysterectomy, or removal of the uterus, in the United States.

Dr. Donna Day Baird, at the National Institute of Environmental Health Sciences in Research Triangle Park, North Carolina, and her associates conducted the Fibroid Growth Study, designed to measure fibroids in women with symptoms.

Included were 262 tumors in 72 women, ages 24 to 54 years. Thirty-eight subjects were African American and 34 were Caucasian. Fibroid volume was documented by MRI performed four times over a 1-year period.

Typically, the fibroids grew by about 9 percent every 6 months. However, 7 percent of tumors regressed by more than 20 percent.

Growth rates varied even within the same woman and "were not influenced by tumor size, location, body (weight or number of prior pregnancies)," Baird's team reports.

Before age 35, rates of fibroid growth were not associated with subject's race. However, growth rates declined with age only among white women who were older than 35 years of age.

Aside from age and race, the only other factor affecting the growth rate was the number of tumors, with single tumors growing much faster than multiple fibroids.

Based on their findings, the researchers suggest that "it may be possible to extend the follow-up time for assessment of fibroid growth" beyond the current clinical practice of evaluation at 6-month intervals.

"In addition," they write, "if further research supports our findings that tumor growth rates decline in white women as they age, those approaching perimenopause might chose to delay treatment and wait for menopause when tumors are likely to shrink."

SOURCE: Proceedings of the National Academy of Sciences, online December 1, 2008.

http://www.reuters.com/article/healthNews/idUSTRE4B08SY20081201?feedType=RSS&feedName=healthNews

The New York Times
nytimes.com

Q & A

What's the Frequency?

December 16, 2008
By C. Claiborne Ray

Q. Is it dangerous for children to go through metal detectors?

A. "I would be surprised to see health effects that could be discernible," said Christopher J. Portier, associate director of the National Institute of Environmental Health Sciences, "but it has not been studied as well as it could be."

With a school metal scanner, he said, "even if you go through it every day, it is just a few seconds," minimizing risk.

Metal detectors generally fall into the midrange of frequency for electromagnetic devices. Research on power lines, which are extremely low frequency, and on cell phones, at the high end, is not relevant, he said.

"This falls into a middle area, the frequencies of FM, AM and CB radios, where there is much less research and much grayer findings," he said.

At the low end of the midrange, Dr. Portier said, as magnetic fields penetrate the body, extremely small electrical impulses are generated.

"We have never been able to conclusively show any effects from those small pulses," he said.

"Toward the high end of the middle range of frequencies, if the field is really, really strong," he said, "you could get slight microwave heating effects, which would dissipate very rapidly, but that would only occur at thousands to tens of thousands of times stronger fields than in a metal detector."

Dr. Portier said his real concern was with the people who operate and maintain the equipment, especially the X-ray backpack scanners, who are continually exposed. He suggested that they should probably be studied as the canaries in the mine for a clue to anything that might suggest the potential to injure children.

Readers are invited to submit questions by mail to Question, Science Times, The New York Times, 620 Eighth Avenue, New York, N.Y. 10018-1405, or by e-mail to question@nytimes.com.

http://www.nytimes.com/2008/12/16/science/16qna.html?_r=2&ref=science

ScienceNews
MAGAZINE OF THE SOCIETY FOR SCIENCE & THE PUBLIC

EPA should test demasculinizing pollutants collectively, NRC says

Cumulative effects of phthalates and related compounds will be larger than effects measured one chemical at a time, reports a National Research Council panel

By Janet Raloff
Web edition: Thursday, December 18th, 2008

On December 18, a National Research Council panel told the Environmental Protection Agency that sufficient data exist to begin assessing the potential health risks posed by phthalates, among the most ubiquitous pollutants on the planet. At the same time, the NRC panel strongly recommended that the agency adopt a "paradigm shift" in the way it assesses the chemicals' toxicity to humans.

Instead of evaluating each phthalate compound individually, EPA should begin assessing risks from likely combos of these and related chemicals — even if each chemical works differently, according to the panel's new report.

Phthalates are a widely used family of plasticizers and solvents. Owing to the chemicals' presence in plastics, cosmetics, personal care products and even medicines, residues of these chemicals show up in everyone throughout the developed world.

For more than a decade, studies in rodents have been demonstrating that exposures to phthalates early in life can perturb — in some cases derail — development of an animal's reproductive organs (*SN: 9/2/00, p. 152*). Males are most sensitive, largely because these chemicals act as anti-androgens. That is, the chemicals lower concentrations of testosterone, the primary male sex hormone. Especially concerning: In females, phthalates can cross the placenta and pollute the womb.

The NRC panel advocated that EPA assess cumulative risks from all phthalates and other anti-androgenic compounds together — even if the way each pollutant depresses testosterone action or availability results from differing modes of action.

Whether these pollutants pose serious risks to people remains an open question, acknowledged several authors of the NRC report, who took part in a teleconference for the report's release.

EPA didn't ask NRC to assess phthalates' toxicity to humans, notes Deborah Cory-Slechta of the University of Rochester School of Medicine and Dentistry in New York. Instead, EPA asked her panel to evaluate whether sufficient data exist to conduct a human risk assessment. And if so, how should the risks be evaluated: on the basis of single compounds considered separately, as a group evaluated together, or as a group assessed along with additional anti-androgenic agents.

Cory-Slechta says her panel found that there are plenty of data for EPA "to go ahead and do it [a human risk assessment]." But the panel also recommended that when EPA does such an assessment, it should take a sharply different tack from its normal approach.

To Shanna Swan, a phthalate researcher at the University of Rochester, the recommended change in how to calculate the risk of these chemicals "is a big deal. Cumulative risk assessment is the way it *must* be done," she says, "given the dose additivity of these chemicals and the multiplicity of our exposures."

Most people regularly encounter many phthalates, and as a class these compounds tend to have similar impacts. So, even if each of five phthalates had no apparent effects at a particular dose when delivered

individually, coincident exposure to the mix might easily prove to compound the toxicity, the new report explained.

Indeed, published data show that “phthalates can work together at quite low doses,” noted NRC panel member Andreas Kortenkamp of the University of London School of Pharmacy in England. “So if combination effects were not taken into consideration at this level, we would underestimate possible risks.” In fact, he said, his committee’s new paradigm for considering phthalate toxicity cumulatively must inevitably result in findings of higher risks than would have been calculated by assessing each chemical in isolation.

In the new report, NRC concluded that a lifelong testosterone shortfall triggered by phthalate exposures can cause “the variety of effects observed” in animals — including infertility, reduced sperm production, undescended testes, penile birth defects and other reproductive-tract malformations — “if it occurs at times that are critical for male reproductive development.” The most sensitive exposure period: time in the womb.

Indeed, concentrations of phthalates measured in amniotic fluid in the human womb can be “in the range of levels in rat amniotic fluid that gives rise to adverse effects in the offspring,” Kortenkamp said.

However, links to human effects have been quite limited, observes panel member Paul Foster of the National Institute of Environmental Health Sciences in Research Triangle Park, N.C. One exception: a study of infant boys linking phthalate exposure in the womb to a feminization of the anogenital distance — the span separating the gonads and anus (*SN: 6/4/05, p. 355*).

In rodents, this distance is demonstrably longer in males. In fact, researchers depend on this sex-linked distance to visually determine the gender of young rodents.

Follow-up studies are needed with more subjects to test the validity of those preliminary data, Foster says. That said, this phthalates toxicologist points out that the general processes by which these chemicals interfere with sexual differentiation “are common to all mammals. And so, having seen them in rats, one would not expect them not to occur in humans — providing, of course, the exposure was high enough.”

*http://www.sciencenews.org/view/generic/id/39447/title/EPA_should_test_demasculinizing_pollutants_collectively,_NRC_says_*

Panel: EPA must consider effects of chemical barrage

December 18, 2008

By Liz Szabo, USA TODAY

Chemicals that interfere with the male hormone system are so common — and so potentially damaging — that the government should stop studying them one by one and consider their combined effect, an expert panel said Thursday.

Phthalates and other hormone-disrupting chemicals pollute the air, water and dust and are found in hundreds of consumer products — including bug spray, perfume, pesticides, shower curtains, food containers, and plastic toys, according to a report released today from the National Research Council, which advises the government on science policy.

BETTER LIFE: Finding toys free of phthalates and BPA
IN-DEPTH: What you need to know about 'everywhere chemical' bisphenol A

Studies from the Centers for Disease Control and Prevention and independent scientists have found phthalates in virtually everyone, including pregnant women and babies.

The Environmental Protection Agency typically studies the impact of these and other chemicals individually. But that approach may underestimate the effect of being exposed to many different chemicals with similar effects, says the University of Rochester School of Medicine and Dentistry's Deborah Cory-Slechta, chairwoman of the committee that wrote the report.

The best way to protect people — especially infants and fetuses, whose reproductive systems are still developing — is to measure the cumulative impact of this hormonal barrage, Cory-Slechta says. In fact, she says that the EPA should always consider cumulative effects — not just for hormone disruptors, but for all potential toxins.

That will allow the EPA to figure out the maximum level to which humans can safely be exposed and create regulations to protect Americans from exposures that could be harmful, says Sarah Janssen of the National Resources Defense Council, an environmental group. Janssen says she hopes that other government agencies — such as the Food and Drug Administration and the Consumer Product Safety Commission — will also consider the cumulative effect of hormone disruptors in food additives, medical equipment, toys and other products.

"We're exposed to a complex soup of chemicals," Janssen says. "It's a warning we can't ignore."

There's enough evidence to start that assessment right away, instead of waiting until additional studies are finished, Cory-Slechta says.

Although the report focused primarily on phthalates, Cory-Slechta note that other products, such as pesticides used in food, also lower testosterone levels.

Animal and human studies link all of these chemicals to a wide spectrum of problems, from reduced sperm counts to genital malformations. Scientists are also studying the chemicals' link to testicular cancer and other problems, the report says.

Although most of the research has been done in animals, there's no reason to think that the substances wouldn't affect humans the same way, says report co-author Paul Foster, of the National Institute of Environmental Health Sciences.

But the American Chemistry Council, an industry group, says that considering the risks of so many chemicals that affect male hormones would be "remarkably ambitious" — and maybe impossible.

"This essentially could result in a study without limits, financially or otherwise," says the council's Chris Bryant in a statement.

Lawmakers and business around the world already have taken steps to limit phthalate exposure.

The European Union has restricted phthalates in cosmetics and children's toys. A growing number of hospitals are phasing out phthalates in neonatal intensive care units, hoping to protect premature and sickly newborn boys.

Congress last summer passed a ban banning several phthalates in children's products. The Consumer Product Safety Commission has said that it will allow stores to continue selling toys made with phthalates, as long as they were manufactured before the law takes effect Feb. 10th.

http://www.usatoday.com/news/health/2008-12-18-phthalates-chemicalsoup_N.htm

REUTERS

Pain pills may cut risk of bowel cancer: study

Fri Dec 26, 2008 9:33am EST

By Joene Hendry

NEW YORK (Reuters Health) - Use of a non-steroidal anti-inflammatory drug (NSAID) for over 5 years may lessen a person's risk of developing cancer of the lower portion of the large bowel, study findings suggest.

This risk reduction appears more robust among whites than among African Americans, Dr. Sangmi Kim, of the National Institute of Environmental Health Sciences in Research Triangle Park, North Carolina, and colleagues found.

The investigators evaluated use of NSAIDs (i.e., aspirin, ibuprofen, and selective COX-2 inhibitors, taken to ease pain and inflammation) among 1,057 white and African American men and women with cancer of the lower bowel and rectum and 1,019 individuals who were cancer-free.

The participants with cancer included 790 whites and 267 African Americans, of whom 76 percent reported ever using NSAIDs during the 5 years prior to diagnosis. Of the cancer-free group, 83 percent reported NSAID use during the 5 years prior to study participation.

Compared with those never using NSAIDs, NSAID use was associated with about 40 percent reduced risk for cancer in the lower portion of the large bowel overall, after allowing for age, gender, race, body mass, physical activity, and other factors potentially associated with distal large bowel cancers.

In analyses that factored for race, the investigators found a "strongly protective" association between NSAIDs and large bowel cancer in whites, according to a report in the American Journal of Epidemiology.

"However," Kim told Reuters Health, "the risk reduction associated with NSAID use was less evident among African Americans."

Risk reduction was slightly stronger with prescription, rather than non-prescription NSAID use, but again this association was stronger among whites than among African Americans.

The apparent protective effect between NSAID use and cancer of the lower portion of the large bowel noted in this study is similar to that previously reported between NSAIDs and colon cancer.

Nonetheless, Kim and colleagues say more study is needed before recommending NSAIDs for the prevention of colorectal cancer in the general public.

SOURCE: American Journal of Epidemiology, December 1, 2008

http://www.reuters.com/article/healthNews/idUSTRE4BP20820081226

Online publication October 21, 2008, actual publication December 1, 2008:
http://aje.oxfordjournals.org/cgi/reprint/168/11/1292

washingtonpost.com

Climate Change May Boost Contact With Pollutants

Friday, December 26, 2008; 12:00 AM

FRIDAY, Dec. 26 (HealthDay News) -- Global climate change may lead to a rise in health problems due to increased exposure to harmful air pollutants, suggest researchers who reviewed studies projecting the impact of climate change on air quality.

The review authors also concluded that reducing greenhouse gas emissions could help reduce the harmful effects of climate change.

The review looked at how climate change will affect ground-level ozone, a known pulmonary irritant that affects the respiratory mucous membranes, other lung tissues, and respiratory function. Exposure to elevated levels of ozone is associated with increased hospital admissions for asthma, allergic rhinitis, pneumonia, chronic obstructive pulmonary disease (COPD), and other respiratory diseases.

"Projections suggest that climate change will increase concentrations of tropospheric ozone, at least in high-income countries, when precursor emissions are held constant, which would increase morbidity and mortality," wrote review authors Kristie L. Ebi and Glenn McGregor. "The potential impact of climate change on ozone concentrations have not been projected for low-income countries, many of which currently have significantly higher ozone exposures."

The authors said further research is needed to better project the health impacts caused by changing concentrations of ozone caused by climate change. They said areas of uncertainty include the projected degree of future climate change, the impact of future emissions and their pathways, potential changing weather patterns, severity of episodes of poor air quality, and changes in population vulnerability.

The review findings were published in the journal *Environmental Health Perspectives*. According to journal editor-in-chief Hugh A. Tilson: "As we reduce vehicle-based emissions of pollutants, urban concentrations of ozone will also be reduced, thereby positively protecting the health of humans for generations to come."

In 2000, urban air pollution caused 800,000 deaths and resulted in 7.9 million disability-adjusted life-years lost due to respiratory problems, lung disease and cancer, according to the World Health Organization.

More information

The World Health Organization has more about climate change and health.

SOURCE: *Environmental Health Perspectives*, news release, December 2008

http://www.washingtonpost.com/wp-dyn/content/article/2008/12/26/AR2008122601247.html

Article: http://www.ehponline.org/docs/2008/11463/abstract.html

The Huffington Post

David Kirby
Posted January 8, 2009 | 02:35 AM (EST)

UC Davis Study: Autism is Environmental (Can We Move On Now?)

I have always said there may be a small percentage of people with autism spectrum disorder (perhaps those with Asperger Syndrome) whose symptoms are a result only of their genetic makeup, with no environmental factors involved at all.

But a new study out of UC Davis' MIND Institute says that it's time to abandon science's long, expensive, and not very fruitful quest to find the gene or genes that cause autism alone, without any environmental triggers.

"We need to keep (environmental) studies going," Irva Hertz-Picciotto, the co-author of the study and professor of environmental and occupational health and epidemiology at UC Davis, said in a statement.

"We're looking at the possible effects of metals, pesticides and infectious agents on neurodevelopment," Hertz-Picciotto said. "If we're going to stop the rise in autism in California, we need to keep these studies going and expand them to the extent possible."

Autism is predominantly an environmentally acquired disease, the study seems to conclude. Its meteoric rise, at least in California, cannot possibly be attributed to that shopworn mantra we still hear everyday, incredibly, from far too many public health officials: It's due to better diagnosing and counting.

The autism epidemic is real, and it is not caused by genes alone: You cannot have a genetic epidemic. It really is time that we, as a society, accept that cold, hard truth.

"It's time to start looking for the environmental culprits responsible for the remarkable increase in the rate of autism in California," Dr. Hertz-Piccotto said.

The study results suggest that "research should shift from genetics, to the host of chemicals and infectious microbes in the environment that are likely at the root of changes in the neurodevelopment of California's children," the statement added.

The UC Davis Study, funded in part by the National Institute of Environmental Health Sciences (NIEHS) found that the rate of autism among six-year-olds in California mushroomed from less than 9 per 10,000 among the 1990 birth cohort, to more than 44 per 10,000 for kids born in 2000.

This increase, "cannot be explained by either changes in how the condition is diagnosed or counted," the statement said, "and the trend shows no sign of abating."

(It is important to keep in mind that almost every child born in 2000 would have received many vaccines that contained the mercury preservative thimerosal, which was not completely phased out of most - but not all - childhood vaccines until at least 2003.)

Of the 600-to-700 percent increase in autism reported in California between 1990 and 2000, fewer than 10 percent were due to the inclusion of milder cases, the study found, while only 24 percent could be attributed to earlier age at diagnosis.

There was only one logical conclusion: some thing or things in the environment had to be at play here.

I have always said that all environmental factors should be considered in at least some subgroups of autism. This position has been met with considerable ridicule. I believe that opponents are afraid that, if we start looking at toxins like heavy metals, it might one day lead back to thimerosal. Likewise, if we consider live virus triggers, we may have to take another look at the measles-mumps-rubella vaccine (which thousands of parents swear was the trigger than sent their children tumbling into autism).

Now, it's always been easier and more reassuring to tell ourselves that autism was almost purely genetic, that it was always with us at the rate of 1 in 90 men (1 in 60 in New Jersey) and that, gee, weren't doctors doing a great job these days of recognizing and diagnosis this disorder.

This pathetic groupthink has helped create hugely lopsided funding priorities in autism, where genetic studies get lavishly funded, while environmental ones are lucky to even pick up the dollar scraps left behind

"Right now, about 10 to 20 times more research dollars are spent on studies of the genetic causes of autism than on environmental ones," Hertz-Picciotto said. "We need to even out the funding."

I agree.

Yes, we must continue to look for the susceptibility genes that make some kids more vulnerable to environmental triggers - possibly through a diminished capacity to detoxify themselves.

But the sooner our best minds in science and medicine come to grips with the fact that these poor, hapless kids have been exposed to the wrong environmental toxins and/or infectious agents at the wrong time, the sooner we can find out how to best treat what really ails them.

It is illogical for us to oppose the study of, say, mercury exposures and autism, because it might somehow implicate thimerosal, and by extension, vaccines.

After all, heavy metal studies into autism could very well incriminate background environmental sources, but exonerate metal sources found in vaccines, such as mercury and aluminum.

And that would be a good thing for everyone.

- *http://www.huffingtonpost.com/david-kirby/uc-davis-study-autism-is_b_156153.html*

tably lead to unapproved pharmaceuticals adulterating the food supply.''

In November, a coalition of 26 environmental advocacy groups, including the Center for Food Safety and the Natural Resources Defense Council, urged the incoming administration to ban the use of food crops to produce medical drugs because they pose ''a long list of risks to health.''

But BIO's Bomer Lauritsen said pharma-crops provide ''very important medical benefits'' and are ''very strictly regulated.''

''We're very supportive of [research and development] for plant-made pharmaceuticals,'' she said.

Schechtman, the USDA biotechnology coordinator, said his agency is ''committed to ensuring field trials [are] done safely.''

He noted that its *Guidance for Industry: Drugs, Biologics, and Medical Devices Derived from Bioengineered Plants for Use in Humans and Animals* provides the biotechnology industry with direction on developing such plants.

APHIS plans to work on establishing a new regulatory category for importing plants awaiting risk assessments in 2009. It plans to issue a notice of proposed rulemaking on this issue in February.

Rulemaking on PIPs Scheduled for 2009. The Environmental Protection Agency will continue working on new data requirements for producers of plant-incorporated protectants (PIPs).

Those potential new requirements include defining the nature of regulated production of PIPs and associated issues such as reporting, product labeling, and recordkeeping, according to EPA's fall 2008 regulatory agenda. The rule is expected to clarify the legal requirements of these products at various phases of production, it said.

EPA said it also plans to address activities that it does not believe warrant regulation and will consider exempting those activities from Federal Insecticide, Fungicide, and Rodenticide Act regulation.

According to the regulatory agenda, the agency plans to issue a notice of proposed rulemaking in September.

Biotechnology Developments in Works. Bomer Lauritsen said the biotechnology industry is expanding development of stacked traits—combinations of built-in features such as insect and herbicide resistance, drought tolerance, and crops that use nitrogen more efficiently to reduce the amount of fertilizer needed to grow them.

Researchers are also working on ways to fortify some food plants with higher nutritional content, she said.

But Greg Jaffe, director of the biotechnology project at the Center for Science in the Public Interest, told BNA that agricultural biotechnology developments will probably be ''variations on a theme'' in the near future—focusing on herbicide tolerance and pest protectants.

There is likely to be greater stacking of genetically engineered traits because that seems to be a big moneymaker, Jaffe noted.

BY BILL PRITCHARD

Science Policy

Nanotechnology Funding, Toxicology Changes, Air Pollutant Assessments to Be Priorities

Passage of legislation to reauthorize funding for the National Nanotechnology Initiative, research to transform toxicology, required evaluations of the hazards of air pollutants, studies of nanomaterials, and priority-setting for research in general will be among the priorities for federal agencies dealing with chemicals in 2009.

E. Clayton Teague, director of the National Nanotechnology Coordinating Office, said he expects legislation to reauthorize the 21st Century Nanotechnology Research and Development Act (Pub. L. No. 108-153) to be approved by Congress in 2009.

Reauthorization of the legislation will continue to provide funding for nanoscience research, which is expected to transform many industries and to create many jobs.

Modernizing Toxicology. Senior officials at the Environmental Protection Agency and the National Toxicology Program (NTP) expect to continue to take steps toward developing quick, cost-effective tests to identify chemical and pollutant hazards.

Early in 2009, EPA will publish an analysis of how well its ToxCast™ robotic system has worked for testing more than 400 ways a chemical affects the body, said Robert Kavlock, director of EPA's National Center for Computational Toxicology. The agency will compare the results of the ToxCast screenings with information from traditional toxicity tests.

The agency has used ToxCast to test more than 300 chemicals, primarily pesticides with rich data sets from traditional toxicology tests, Kavlock said. The goal is to see whether ToxCast identifies ''signatures'' or patterns of biological response that will predict toxicity.

Kavlock expects the results to be published in a peer-reviewed journal in March or April. EPA will hold a workshop in May to examine various ways to analyze the ToxCast data.

The National Center for Computational Toxicology will launch the second phase of its ToxCast analysis in 2009 by testing a larger and more diverse set of chemicals, Kavlock said. For example, the agency will work with a pharmaceutical company to obtain 100 medicines that have failed in clinical trials, Kavlock said. The medicines will be put through the ToxCast screening process to determine how they caused harm.

Testing 10,000 Chemicals a Week. In addition to the second phase of ToxCast, Kavlock said the National Center for Computational Toxicology will work with NTP and the National Institutes of Health's Chemical Genomics Center, which uses robotic technologies to study protein and cell function along with genetic responses to chemicals. The NIH Chemical Genomics Center uses equipment that can perform two tests on more than 10,000 chemicals in a week, he said.

The agencies anticipate studying thousands of chemicals by the summer of 2009, Kavlock said.

John Bucher, NTP's associate director, said the tests will evaluate a range of biological effects and different concentrations of the chemicals.

Top Science Policy Issues in 2009

The issues that will dominate the science policy agenda in 2009 include:

- reauthorization of the National Nanotechnology Initiative,
- transformation of toxicology research at EPA, and
- evaluation of the hazards of air pollutants.

In addition, the computational toxicology center is working with nearly two dozen laboratories to develop additional high-throughput screening tests, Kavlock said.

The laboratories test chemicals ToxCast already has evaluated in order to determine how well their tests work, Kavlock said.

''This will be an amazing data set,'' Kavlock predicted.

Peter Preuss, director of EPA's National Center for Environmental Assessment, said his office will seek to determine how the data generated by ToxCast and other high throughput screening tests can be used in risk assessments.

He said the NIH Chemical Genomics Center will be evaluating phthalates with ToxCast, and the National Center for Environmental Assessment expects to compare that data to information it has from traditional tests.

''I think 2009 will be a very important year in terms of taking some of those [alternative] studies and thinking through how we use them in risk assessment,'' Preuss said.

Nanomaterial Toxicity Tests. In 2009, the ToxCast system also will be used to test nanomaterials.

EPA will test 14 nanomaterials that the Organization for Economic Cooperation and Development (OECD) is evaluating through a comprehensive, traditional toxicity testing program, said Jim Willis, director of EPA's Chemical Control Division and chairman of OECD's Working Party on Manufactured Nanomaterials.

The OECD, comprising 30 of the world's industrialized nations, launched a multilateral program in 2007 to test the safety of 14 manufactured nanomaterials, including nanoengineered buckyballs, carbon nanotubes, and nanoscale silver and iron.

The results of the traditional tests on the nanomaterials will help EPA to learn how well ToxCast predicts any harmful effects, Willis said.

Charles Auer, who recently retired as the head of EPA's Office of Pollution Prevention and Toxics, said it is vital to have the robotic assessments the National Center for Computational Toxicology is developing used for nanomaterials because the materials are so expensive that it is cost-prohibitive to secure the quantities needed for animal tests.

Regarding animal testing, Troy Seidle, senior adviser for science policy for three Humane Society organizations, said he anticipates a number of developments in cellular studies in 2009.

European regulators are expected to adopt three in vitro methods that will fully replace animals used for skin irritation tests, Seidle said.

''This will represent the first case in which an animal test is fully replaced by non-animal test methods,'' he said.

Seidle said the next step will be to work toward having OECD accept the non-animal tests. Once accepted by OECD, the non-animal tests effectively will be globally accepted, he noted.

Studying Genetic Susceptibility. In addition to working with EPA to further define chemical toxicity, Bucher said, NTP will continue its Host Susceptibility Program, which seeks to understand the genetic basis for why some individuals are more susceptible than others to some substances in the environment.

Asthma, heart disease, cancer, and diabetes are examples of diseases thought to be affected by genetic susceptibility and environmental exposures, according to NTP. It is working with universities to examine strains of mice to see how small genetic differences change their response to environmental agents, Bucher said.

NTP hopes the information from the high throughput screening and host susceptibility programs will be able to identify genetic factors that govern susceptibility to environmental exposures, he said.

Air Pollutant Studies Required. Preuss of NCEA said his office's top priority in 2009 will be meeting court-ordered deadlines to evaluate the health hazards of criteria air pollutants.

The Clean Air Act requires EPA to reassess every five years the health risks of six common air pollutants—particulates, ground-level ozone, carbon monoxide, sulfur oxides, nitrogen oxides, and lead.

The agency has been sued for missing deadlines for all of the criteria pollutants except particulates, Preuss said.

''As a result we have a court-ordered deadline for nearly every criteria air pollutant,'' he said. Many of those deadlines are in 2009 and 2010, Preuss said.

In the past, the National Center for Environmental Assessment has focused on one criteria air pollutant at a time, but this year, the agency will work on all six simultaneously, Preuss said. ''That will be the top priority for NCEA in 2009.''

In addition to working on the criteria air pollutants, the National Center for Environmental Assessment expects to release in 2009 draft toxicological reviews of several high-profile chemicals including trichloroethylene and formaldehyde, Preuss said.

Preuss also said the agency will determine how it will respond to a National Academies report issued in December, *Science and Decisions: Advancing Risk Assessment*, criticizing the EPA risk assessment process as bogged down by funding and staff shortages and saying its current approach to scientific uncertainty contributes to decisionmaking gridlock.

In the past, it sometimes has taken EPA more than a year to respond to National Academy recommendations.

Global Assessment of Nanotechnology. EPA's Willis, who also chairs OECD's nanomaterials working party, said a number of countries, including China, Russia, and Thailand, already have volunteered to test 10 of the 14 nanomaterials OECD is targeting.

Neither of the three countries is a member of OECD.

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''It's great to see this kind of international cooperation on issues of mutual importance,'' Willis said.

The countries will test the selected nanomaterials for 59 different types of environmental, health, and safety effects they might have, Willis said.

By March, the working party hopes to release a database of nanomaterials research being conducted by both countries, and hopefully some companies, around the world, Willis said.

That database will help OECD, individual countries, and companies to shape a strategic plan to research the environmental, health, and safety questions surrounding engineered nanomaterials, he said.

The OECD working party will develop test guidelines and other documents through a ''wiki'' format so that the guidance can be updated as new information becomes available, Willis said.

In conjunction with the OECD efforts, Teague of the National Nanotechnology Coordinating Office said he expects academic, corporate, professional, and nongovernmental organizations to agree in 2009 on a base set of physical and chemical characterizations to describe nanomaterials, which will be particularly useful for toxicological studies.

Willis added that the OECD working party will host a conference on the environmental benefits of nanotechnology to take place in Prague in June. Some of the benefits include improving the collection of solar energy, improving battery technology, cleaning groundwater, and improving the energy efficiency of building materials.

Setting Agency Research Priorities. EPA's Chief Scientist Pai-Yei Whung said she will work with the Science Policy Council, which consists of the agency's top scientists, to set priorities for the research EPA will conduct in 2009 and beyond.

Issues the council is considering include climate change, energy, future contaminants, homeland security, and pollution prevention, Whung said.

EPA's Risk Assessment Forum, a committee of senior EPA scientists established to promote consensus on risk assessment issues, will be working to integrate its environmental and human health risk assessments, Whung said.

Currently, the agency's ecological risk assessments and human health risk assessments are separate documents, she said. It will take time to combine them, but it will be important to do so, Whung added.

Whung said EPA will be developing a Climate Change Technology Activity Database to collect and analyze the work under way in various agency offices. The database is intended initially for internal use to determine where there may be gaps in EPA's research, she said. But, after appropriate review, Whung said, it could be used for a cross-federal needs assessment.

David Rejeski, director of the Synthetic Biology Project and Project on Emerging Nanotechnologies, took an overarching view of how the incoming administration should address technology generally.

Rejeski noted that the National Academies' report, *Review of Federal Strategy for Nanotechnology-Related Environmental, Health, and Safety Research*, found in December that the federal government lacked a national strategy to address environmental, health, and safety questions arising from nanotechnology.

''The next administration needs to put in place the people and institutions to finally, and effectively, make public policy on the technological frontier,'' Rejeski said.

BY PAT RIZZUTO

DISCOVER

Is One Very Tough Rat a Very Big Risk to Human Health?

The rodents charged with testing environmental chemicals may be too tough for their jobs.

January 21, 2009
by Marilyn Berlin Snell

The success of one of the most ambitious and contested federal science programs in years may rest on the delicate shoulders of a one-pound albino breed of rat known as Sprague Dawley. In a hotly debated move, the U.S. Environmental Protection Agency (EPA) has selected this unassuming rodent as the primary test animal for a vastly complex and comprehensive new chemical-evaluation program. The effort is designed to investigate many of the most vexing public-health questions of the day: Are you putting yourself, your children, or even your children's children at risk when you microwave food in plastic containers? What is contributing to hormone-related killers like breast, uterine, and testicular cancer? And are common garden sprays—like the one you use to keep the aphids off your hybrid tea rose—affecting your unborn baby's developing brain?

The EPA initiative, called the Endocrine Disruptor Screening Program, is set to begin testing some of the 87,000 chemicals identified by a federal advisory panel for their potential to interfere with the body's endocrine, or hormone, system. As the body's chemical messengers, hormones play a critical role in regulating biological processes including metabolism, reproduction, and brain development. The female ovaries, male testes, and pituitary, thyroid, and adrenal glands are all part of this complex system. Endocrine disruptors may mimic natural hormones or block their normal action, cause the body to produce too much or too little of a hormone, or scramble a hormone's message so that the body thinks it should abort a fetus, for example, or produce extra insulin. If any of the thousands of chemicals in common use today adversely affect the human hormone system, the EPA's testing program should catch them—but only if Sprague Dawley catches them first. And therein lies the controversy.

Since World War II, this white-furred rodent with beady red eyes has been among industry's most often used lab rats for testing drugs and chemicals before they hit the market. The animal's utility is undisputed; it has helped researchers study not just pharmacology and toxicology but everything from cancer and AIDS to obesity and aging. In this case, though, it may be the wrong rat for the job. Critics say that Sprague Dawley is a kind of superrodent whose hearty constitution may not react in ways an average human's would. If so, the animal could give a clean bill of health to chemicals that actually pose a real threat to human well-being.

Last spring the EPA convened a scientific advisory panel to make final adjustments to the proposed testing program. One panelist was David Furlow, a University of California at Davis endocrinologist with extensive experience in rat-strain variations and how they can affect outcomes in the lab. He tried repeatedly to raise a red flag about Sprague Dawley. "I've known about these differences since I was an undergraduate in the 1980s," Furlow says, citing scientific literature that suggests it is more resistant to endocrine-disrupting chemicals than other rat strains. His concerns, he says, were downplayed.

Sprague Dawley's unique characteristics have been evident for decades. In 1946 physical chemist Robert Dawley's company sent a letter to the National Institutes of Health (NIH) detailing how, through selective breeding, Dawley had developed a rat (Sprague was his first wife's maiden name) with good temperament, vigor, and high rates of lactation. But Sprague Dawley's good genes—not to mention its fecundity—could have bad consequences for humans: A prolific breeder may not be the best test subject for chemicals that may cause infertility and other reproductive problems. The letter to the NIH also stated that the rat strain had been bred for "high resistance to arsenic trioxide," a toxic substance used in insecticides and herbicides and known today to be an endocrine disruptor.

"It's a significant problem," says Jef French, acting chief of the Host Susceptibility Branch of the National Toxicology Program at the National Institute of Environmental Health Sciences. (French emphasized that he was speaking for himself and not the government.) "Because of Sprague Dawley's [genetic] selection, chemicals that might be harmful to humans might be judged to be nonharmful to the rat," he says.

The results of the EPA's tests could guide federal regulation of numerous chemicals for many years to come, so the stakes for both the public and the chemical industry are enormous.

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The far-reaching Endocrine Disruptor Screening Program dates to 1996, when Congress ordered the EPA to begin testing chemicals for their potential to interfere with the human endocrine system. By some accounts the legislation was prompted by the publication earlier that year of a book titled *Our Stolen Future*. Called "an environmental thriller" by *The Washington Post*, the book, by two zoologists and an environmental journalist, called attention to a longtime concern of environmentalists: failing wildlife populations and strange deformities in the offspring of those that survived. For instance, there was a massive die-off of alligators after a 1980 pesticide spill in Florida's Lake Apopka. Studies later found deformed sex organs in the offspring of the remaining gator population, even after tests showed the water in the lake to be apparently clean. Mink ranchers in the Great Lakes region who fed their animals local fish began noticing that the females weren't producing pups, a problem later linked to PCB contamination. In California researchers found what came to be known in the press as "gay gulls": same-sex seagull couples shacking up together in the nest, protecting eggs with abnormally thin shells that often harbored dead chicks. DDT was the suspected culprit.

Because of genetic selection, chemicals that might be harmful to humans might be judged nonharmful to the rat.

Confronted with these findings, scientists began to wonder whether small quantities of synthetic chemical compounds found in our food and water—and in everyday products like makeup, plastics, and bug spray—could be sabotaging human fertility, undermining our immune systems, or affecting prenatal development. When the public got wind of the possible threat and started demanding answers, the EPA's Endocrine Disruptor Screening Program was born.

Twelve years and $76 million later, not a single chemical has been screened by the EPA for its potential to scramble male, female, and thyroid hormones. Before screening could begin in earnest, the agency had to make sure that the protocols used in the screens would be reliable and reproducible. In this validation phase, studies were conducted at several labs using the same protocol, with the results then compared to ensure that the screens are replicable across labs. In this preliminary phase, several rat strains were used, including ones known as Long-Evans Hooded and Wistar, but Sprague Dawley was always the top pick.

During the validation studies, Sprague Dawley and other strains were housed in polycarbonate cages with wire lids. In some tests their life spans were brief—around six to eight weeks. Juvenile males were dosed with chemicals, then decapitated and examined. Pubescent males and females were injected with atrazine and myriad other chemicals, then had ovaries removed and studied, tiny testicles weighed, and kidney and thyroid glands checked for toxic effects.

A 2003 white paper commissioned by the EPA notes that because companies have for decades conducted these kinds of tests on Sprague Dawley, there is a large database of information on them that is lacking for other strains. But a "reviewer's appendix" to the white paper—in which an independent scientist is asked to critique the report—argues that Sprague Dawley may be a poor choice for endocrine disruptor screening because the animal was bred to be resistant to known environmental toxicants. Written by research geneticist Jimmy Spearow, then at U.C. Davis, the appendix presented evidence that other rat strains, including Fischer 344, were more sensitive to more chemicals than was Sprague Dawley. "Compared with several other strains that have been studied, the strain that is least sensitive to the most endocrine-disrupting chemicals has been identified, and the EPA is planning to use it in the screening assays," says Spearow, now a staff toxicologist for the California EPA; he emphasizes that this is his personal opinion, based on previous work conducted at Davis. In 2007 the EPA finally acknowledged there was reason to believe that Sprague Dawley might be less sensitive to certain endocrine tests, which made critics like Spearow wonder what other toxic effects the rat had failed to catch all those years.

Which rat to use in the EPA study isn't the only thing being fought over. There has been a pitched battle between the chemical industry and its many critics regarding the Endocrine Disruptor Screening Program itself, with some industry representatives questioning the very premise that endocrine disruption is a human health risk. At a recent industry-sponsored workshop on the endocrine disruptor program that included representatives from Procter & Gamble, Monsanto, the American Chemistry Council, and Dow, one speaker repeatedly prefaced the phrase "endocrine disruptor" with "quote unquote."

"There will always be different interpretations of science," says Angelina Duggan, an original member of the EPA advisory panel and today a managing scientist at Exponent, a chemical industry consulting firm. "Whether this issue is more emotion or science remains to be seen."

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To Marion Moses, a physician who runs the Pesticide Education Center in San Francisco, there is no need for such equivocation. "It's become a fight over process and whether one can extrapolate animal studies to humans," she says. "It's a charade, and it has been going on for 12 years." Trying to nail down unassailable proof of endocrine disruption

in humans is essentially a fool's errand, in her view. Moses, who has treated farmworkers for acute poisoning, rashes, and asthma that seem to be related to the spraying season, feels that the wildlife data alone should be enough to outlaw certain pesticides. "I spent a lot of time trying to get these awful chemicals off the market," she says while walking in a San Francisco garden-supply store. The snail bait, lawn weed-and-feed products, fungicides, and insect repellents she pulls off the shelf all contain chemicals slated for testing.

The 2003 white paper that drew such strong criticism from Spearow, who called it "disturbing" and "misleading," was coauthored by Rochelle Tyl, another member of the EPA advisory panel. Tyl, who runs a lab in North Carolina's Research Triangle Park where many of the screens and tests will eventually be done, acknowledges that Sprague Dawley isn't the perfect choice. Still, she defends the report, calling Fischer 344, for instance, a "lousy" test animal because the males have reproductive problems. Asked about rats bred to be super reproducers, she waves her arm impatiently. "I know that's the criticism, that Sprague Dawleys are good breeders. But if you don't have an animal that gives decent litters, how do you run a study?"

Gary Timm, a senior environmental scientist with the EPA, has been working on the endocrine disruptor program since its very first days and likewise recognizes the complexity of the process. "I've been totally surprised at how long it's taken," he says. The agency felt a constant tug between "keep it simple" and "be comprehensive."

"Compromises have been struck," Timm continues. He, too, cites the problem of Sprague Dawley's virility. "People say, 'Look, these rats suffer a 50 percent decrease in sperm and they still reproduce.' They say, 'If you had a guy who had a 50 percent decrease in sperm, he'd be infertile!'" Asked how he responds to such criticism, he answers, "Those are just some of the things we have to allow for."

Representative Henry Waxman and others on the House Committee on Oversight and Government Reform are not so sure. In 2007 the committee sent a letter to the administrator of the EPA voicing concern that public health was being put at risk by the selection of Sprague Dawley. The agency responded, "While the EPA recognizes there are reasons to believe that this strain might be less sensitive, the data currently available appear to show that it is no worse (or better) than other strains for screening for endocrine activity."

In some ways the EPA is correct, Spearow says. No one rat strain is most sensitive to all endocrine-disrupting chemicals. "However, available data show that the Sprague Dawley rat strain is least sensitive to the most endocrine-disrupting chemicals relative to other strains that have been studied," he says. "I'm not saying it is inappropriate for all testing, but to use it as the only test animal in this program means that we could really underestimate the effects of certain kinds of chemicals. Do we make sure they're safe for King Kong? Or do we make sure they're safe for you and me and Bambi?"

Congress, fed up with the EPA's delay of more than a decade, wrote into the 2008 appropriations bill that the screening of possible endocrine-disrupting compounds was to begin last summer. Testing of the first chemicals, including the herbicides 2,4-D and atrazine and the insecticide malathion, was scheduled to follow, but the EPA pushed back its deadlines yet again, to early 2009.

Endocrine disruption, with its diffuse causes and effects that may not show up for a generation, is a hydra-headed 21st-century health challenge. Thousands of chemicals will be tested and many millions of dollars will be spent. Still, opponents of using Sprague Dawley say one nagging question remains: If the whiskered workhorse in the laboratory isn't up to the task, who will be the real lab rats?

washingtonpost.com

Database Helps Assess Your Breast Cancer Risk

By Serena Gordon
HealthDay Reporter

Sunday, January 25, 2009; 12:00 AM

(HealthDay News) -- If you want to learn more about the key risk factors for breast cancer, such as obesity, pollutants or smoking, a database can guide you to the available evidence that confirms or quells an association.

"Breast cancer is multifactorial. It would be rare for there to be a single environmental chemical that alone would be sufficient to cause an increase in breast cancer," said Dr. Robert Schneider, co-director of breast cancer research at New York University School of Medicine in New York City.

"In many cases, an increased risk of breast cancer is quite small, and we don't yet know how each factor affects the risk of breast cancer," he said, explaining that it's similar to a puzzle. "We need to know how all of the pieces fit together, and this database begins to help us start assessing some of that."

The database, a joint project of Susan G. Komen for the Cure and the Environmental Factors and Breast Cancer Science Review project led by the Silent Spring Institute, includes information on 216 chemicals, diet, smoking, physical activity and weight that may play a role in the development of breast cancer.

Fewer than 100 chemical compounds have been identified as human carcinogens by the International Agency of Research on *Cancer*. However, that doesn't mean that all other chemicals are safe, just that they haven't been tested. And, an estimated 80,000 chemicals have been registered for commercial use in the United States, according to the database study, which was published in a recent issue of the journal Cancer.

Although many factors have been associated with breast cancer, Schneider said his top three would include the chemical bisphenol A, radiation exposure from CT scans and delayed first pregnancy.

Bisphenol A (BPA) is an estrogenic chemical found in many products made of polycarbonate plastic (clear, hard plastic), such as baby bottles, reusable water bottles, food storage containers, food cans and water supply pipes, according to the National Institute of Environmental Health Sciences. Although no human studies have confirmed an association with breast cancer, a study done in mice suggests there may be a link. However, the U.S Food and Drug Administration recently said the agency felt there were "adequate margins of safety" for the chemical in the amounts commonly consumed.

"We don't know what constitutes an unacceptable level," said Schneider who would prefer to err on the side of caution and limit BPA exposure, especially in infants and young girls.

Schneider said another concerning risk factor is the amount of radiation people are exposed to for routine health problems, particularly from CT scans.

Although the last risk factor from Schneider's top three -- delayed first pregnancy -- isn't one people are likely to change, he said it's important to be aware of it. "In a modern society, it's exceedingly difficult to have a pregnancy before 20 when it would be quite protective," said Schneider.

Dr. Jay Brooks is chair of hematology/oncology at Ochsner Health System in Baton Rouge, La. He said, "When you look at environmental and chemical risk factors, you have to remember that we live in a sea of chemicals, and those chemicals have made our lives so much nicer, and it's hard to know exactly what each one does to an individual's risk.

"I advise my patients to try to control the things you have good control over. Weight is a huge issue in breast cancer, as is the use of combined estrogen/progesterone after menopause," he added.

Brooks said extra weight is a risk factor that many women underestimate, but being overweight clearly increases risk. And, he said, estrogen therapy alone used to ease menopausal symptoms doesn't seem to increase risk the way the estrogen/progesterone combination does.

More information

To learn more about breast cancer risk factors, check the searchable database from the Silent Spring Institute.

SOURCES: Robert Schneider, Ph.D., co-director, cancer research, New York University School of Medicine, New York City; Jay Brooks, M.D., chair, hematology/oncology, Ochsner Health System, Baton Rouge, La.

http://www.washingtonpost.com/wp-dyn/content/article/2009/01/25/AR2009012500665_pf.html

javmaNews

February 1, 2009
by Katie Burns

Training program brings veterinary pathologists to NIH

Participants complete residencies at veterinary colleges, dissertation work at National Institutes of Health

Genetic causes of breast cancer and leukemia were the topics of dissertations by the first two veterinary pathologists to complete a joint training program between the National Institutes of Health and five veterinary colleges.

The NIH recently held a symposium to highlight the program's early progress and participants' contributions to biomedical research. The Comparative Biomedical Scientist Training Program Symposium took place Oct. 2-3, 2008, on the NIH campus in Bethesda, Md.

The National Cancer Institute launched the veterinary training program in 2003, and four other NIH institutes have joined. The NCI has partnered with the veterinary schools/colleges in Illinois, Indiana, Maryland, Michigan, and North Carolina. Ten veterinarians are training in the program, which starts with a pathology residency at one of the veterinary colleges and ends with dissertation work at an NIH institute.

"It provides us the opportunity to train additional pathologists for a global need," said Dr. John Cullen, who directs the program at the North Carolina State University College of Veterinary Medicine.

Dr. Cullen noted that the program combines anatomic and investigative pathology. Also, the program allows veterinarians to develop relationships with other scientists—working together to improve animal and human health so that the idea of "one medicine" is more than an idle concept.

Dr. Willie Reed, dean of the Purdue University School of Veterinary Medicine, said the program specifically helps meet needs for veterinarians in biomedical research and pathologists at veterinary colleges.

"It allows our faculty and students access to cutting-edge research conducted by world-class NIH scientists," Dr. Reed added.

Last year, Drs. Mark Hoenerhoff and David Caudell were the first veterinarians who completed their PhDs through the program.

"As veterinarians and as pathologists, we have a great opportunity to really make a difference in biomedical research through using our knowledge of biological systems to solve problems relating to human health," said Dr. Hoenerhoff, who completed his training at NCI and now conducts research at the NIH National Institute of Environmental Health Sciences.

Dr. Hoenerhoff studied the BMI1 gene in vitro and in mice. The gene can contribute to the development of breast cancer. Dr. Hoenerhoff's team found that overexpression of BMI1 in conjunction with overexpression of Hras, an oncogene commonly overexpressed in a number of cancers in humans, augments tumorigenesis.

Dr. David Caudell focused his work at the NCI on leukemia research in rabbits and mice. Studying the role of chromosomal translocations, Dr. Caudell generated transgenic mice that expressed a CALM-AF10 fusion gene. Almost half the mice developed acute leukemia—providing experimental confirmation that this fusion, isolated from patients with some forms of leukemia, is leukemogenic.

Dr. Caudell said he enjoyed the chance to pioneer the veterinary training program at the NIH. "It's been really great watching the program evolve, watching it grow exponentially."

Dr. R. Mark Simpson, director of the Molecular Pathology Unit within the NCI Laboratory of Cancer Biology and Genetics, was the founder of the training partnerships with the veterinary colleges. He said the NIH institutes benefit from veterinarians' comparative perspectives in problem solving, hypothesis testing, and critical thinking.

Dr. Simpson also received the 2008 Leading Diversity Award from the NCI for recruiting and mentoring African-American veterinarians and veterinary students.

"We have been successful in our ability to include underrepresented minority veterinarians, in large part, due to combined efforts in building a network of supportive programs and people at both the NIH and our veterinary college partners," he said.

Dr. Simpson said the joint training program's ultimate goal is to prepare interdisciplinary, comparative biomedical scientists who will help lead the research teams of the future—opening new synergies to address public health challenges impacting humans, animals, and the environment.

Information is available at http://ccr.ncifcrf.gov/resources/molecular_pathology.

The Arizona Republic

Researchers find way to cut ozone's effects on asthma

by Ginger Rough

Feb. 4, 2009 12:00 AM

Researchers say they may have found a key to treating the ozone-triggered asthma attacks and respiratory problems that plague residents in hot-weather states like Arizona.

A study released Tuesday by the National Institutes of Health shows for the first time how ozone irritates the lungs, findings that could ultimately lead to better treatment options for asthma sufferers.

The report has particularly wide-reaching implications in this state, which not only has one of the nation's highest rates of asthma but struggles to control ozone pollution during the summer months.

"I can't say we found the cause of asthma, but in this instance, we were able to completely get rid of the symptoms," said Stavros Garantziotis, principal investigator with the National Institute of Environmental Health Sciences, part of the NIH. "We were able to stop the irritation (in the lungs)."

Any new drugs or therapies that arise from the research are still years away, he cautioned.

The study, done in conjunction with Duke University, found that mice exposed to so-called bad ozone, a key component of urban smog, produced high amounts of a sugar called hyaluronan.

The sugar was directly responsible for the narrowing or constriction of the animals' airways, a primary cause of asthma symptoms and attacks in humans.

Discovering a clue

"We found that it is not the ozone itself that causes the body to wheeze but the way the lungs respond to (it)," Garantziotis said.

Hyaluronan is found naturally in many tissues of the body, including skin and cartilage, and has been used to treat such conditions as osteoarthritis of the knee.

But researchers found that the mice produced it in a different, more harmful form after being exposed to ozone.

They also discovered they were able to neutralize this "bad" hyaluronan and stop the lungs' airways from narrowing by using several proteins and an altered form of the sugar.

As many as 548,000 state residents suffer from asthma, according to the American Lung Association of Arizona, and studies suggest that Valley's year-round pollution problems exacerbate those symptoms.

Much of the local attention has focused on links between respiratory problems and particulate pollution, the tiny bits of dust and soot in the air.

But ozone is a growing concern for state and local health officials.

In 2008, metro Phoenix exceeded the federal health standard for ozone on 28 days, compared with none in 2007 and nine in 2006.

Part of the jump was due to a tightening of federal standards.

Nationally, the Environmental Protection Agency estimates that ozone-related health problems cost the United States $5 billion a year in premature deaths, hospitalizations and school absences.

"This finding has real-life therapeutic implications," Garantziotis said of the study, which was published in the *Journal of Biological Chemistry*.

Division of Intramural Research

NAEHS Council Update

February 2009

DIR RECRUITMENTS

Investigators in Bioinformatics
The NIEHS is seeking an investigator in Bioinformatics/Computational Biology. Candidates will be considered for Senior Investigator or Tenure-Track Investigator, depending upon qualifications. The incumbent will develop and direct a strong research group to carry out independent and collaborative research in the general area of bioinformatics and computational biology, particularly as related to biological networks, analysis of high-dimensional data, proteomics, comparative and functional genomics, gene expression, and epigenetics. This work will provide a bioinformatic infrastructure and innovative data mining approaches to advance intramural research aimed at understanding biological responses to environmental stressors, in the context of cell biology, animal experimentation, clinical research and epidemiology. Dr. Thomas Kunkel, Laboratory of Molecular Genetics, is chair of the search committee. Candidates have been identified for two Tenure-Track positions.

Tenure-Track Reproductive Epidemiologist
The Epidemiology Branch, National Institute of Environmental Health Sciences, NIH, invites applications for a tenure-track epidemiologist to develop an independent investigator-initiated research program. Applicants must have an M.D. and/or Ph.D. in epidemiology or related field, at least two years of post-degree research experience, and a record of accomplishment, including relevant peer-reviewed publications. Expertise is welcome in areas of reproduction, infertility, pregnancy, child development, and early origins of later outcomes. Research on environmental and/or genetic contributors to outcomes is encouraged. Applicants will be evaluated on their demonstrated ability to conduct biologically-based, interdisciplinary, population-level research in reproductive or developmental epidemiology. Dr. E. Mitch Eddy, Laboratory of Reproductive and Developmental Toxicology, is chair of the search committee. A candidate has been identified for selection.

Staff Scientist in Membrane Signaling
The Laboratory of Neurobiology at the National Institute of Environmental Health Sciences is recruiting a staff scientist on a renewal appointment in the Membrane Signaling Group to organize electrophysiological studies of ion channel regulation by signal transduction pathways. The selectee will independently design, implement, analyze, and trouble shoot patch clamp studies of ion channel regulation and teach patch clamp electrophysiology to other members of the Membrane Signaling Group and members of other research groups within the Division of Intramural Research. Dr. Jim Putney, Laboratory of Signal Transduction, is chair of the search committee. Dr. Christian Erxleben, Laboratory of Neurobiology, NIEHS has accepted the position.

Tenure-Track X-Ray Crystallographer
The Laboratory of Structural Biology in the Division of Intramural Research of the National Institute of Environmental Health Sciences is seeking a Tenure-Track Principal Investigator in X-ray crystallography. Applicants should have a doctoral degree, a clear record of accomplishment in X-ray crystallography, and plans to develop a strong and

original research program to investigate the structure and function of proteins involved in determining biological responses to environmental stress. While applicants proposing research in all areas related to the structure of biological macromolecules will be considered, we are particularly interested in candidates proposing research plans that coincide with areas of strength in the NIEHS Intramural Program, including but not limited to signal transduction, nuclear hormone receptor signaling, epigenetics, DNA replication and repair, and pulmonary biology. Dr. Michael Resnick, Laboratory of Molecular Genetics, is chair of the search committee. Three candidates have been interviewed.

Tenure-Track Embryonic Stem Cell Biologist
The Laboratory of Molecular Carcinogenesis is recruiting a Tenure-Track Investigator - Embryonic Stem Cell Biologist with intellectual and research strengths in, but not necessarily limited to, regulation of gene expression, development, chromatin and epigenetics. The successful applicant will be expected to establish a high-quality independent research program in stem cell biology, relevant to cancer, within a group with diverse research interests and backgrounds but focused upon the molecular and environmental mechanisms of carcinogenesis. Applicants should have a Ph.D, M.D. or equivalent doctoral degree with 3 years of postdoctoral research experience, and a strong publication record. Research experience with cancer models is desirable but not mandatory. Dr. Traci Hall, Laboratory of Structural Biology, is chair of the search committee. Three candidates have been interviewed.

Tenure-Track Developmental Neurobiologist
The Laboratory of Neurobiology is recruiting a Tenure-Track Investigator to lead a high-quality independent research program on any fundamental aspect of developmental neurobiology with the potential for identifying and preventing the deleterious effects of environmental exposures on human cognitive development. Applicants should have a Ph.D., M.D., or equivalent doctoral degree with at least 3 years of postdoctoral research experience in developmental neurobiology and a strong publication record. Applicants using fluorescence imaging and genetic model organisms are particularly encouraged to apply, but the emphasis will be on identifying an outstanding scientist with an innovative research program. Dr. Jan Drake, Laboratory of Molecular Genetics, is chair of the search committee.

Tenure-Track Developmental Biologist
A position is available for a Developmental Biologist to establish an independent basic research program and form a research group in the Laboratory of Reproductive and Developmental Toxicology, Division of Intramural Research. Applications are invited from scientists with demonstrated ability for creative and productive research in cellular and molecular mechanisms of mammalian development. Of particular interest are investigators using rodent models to study cell interactions, epigenetics or other basic biomedical problems relating to the impact of the environment on development. The successful candidate will interact with investigators studying diverse problems in reproductive biology, developmental toxicology, hormone mechanisms, signal transduction, cell cycle regulation, cell growth and differentiation, apoptosis, gene

regulation, mutagenesis and DNA repair, and cancer biology. Minimum qualifications are an M.D., Ph.D., D.V.M. or equivalent doctoral degree in the biomedical sciences, at least three years of postdoctoral experience, and publications in high quality journals. Dr. Darryl Zeldin, Acting Clinical Director and Laboratory of Respiratory Biology, is chair of the search committee.

NEW APPOINTMENTS IN THE DIVISION OF INTRAMURAL RESEARCH

Dr. Raymond Tice, Chief, Biomolecular Screening Branch

Dr. Tice joined NIEHS/NTP in 2005 as the Deputy Director for the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). In late 2008, Dr. Tice was promoted to be the Chief of the recently created NTP Biomolecular Screening Branch (BSB), which administers the NTP High Throughput Screening (HTS) program. The HTS approach will be to screen for the ability of known and suspected toxicants to interact with targets within cellular pathways critical to carcinogenicity, reproductive and developmental toxicity, genotoxicity, neurotoxicity, and immunotoxicity.

The goals of the HTS Program are to (1) prioritize substances for further in-depth toxicological evaluation (to judiciously allocate efforts and resources to maximize public health impact), (2) identify mechanisms of action for further investigation (e.g., disease-associated pathways), and (3) develop predictive models for in vivo biological response (predictive toxicology).

Through a memorandum of understanding, the NTP is partnering with the National Human Genome Research Institute's NIH Chemical Genomics Center (NCGC) and the U.S. Environmental Protection Agency's National Center for Computational Toxicology, to test a large number of compounds (~ 10,000) broadly characterizing and defining the chemical-biological space occupied by chemicals of toxicological concern in selected quantitative HTS assays at the NCGC. Data from these assays, along with full chemical characterization and assay protocol details, are being deposited into publicly accessible relational databases, such as PubChem. Secondary screens using the *Caenorhabditis elegans* model are under development at the NTP and the tripartite collaboration between the NTP, EPA, and NCGC will establish a full spectrum of secondary and tertiary screening assays to further define and characterize activities identified in initial high throughput screens.

Selected Publications

Xia M, Huang R, Witt KL, Southall N, Fostel J, Cho M-H, Jadhav A, Smith CS, Inglese J, Portier CJ, Tice RR, Austin CP. Compound cytotoxicity profiling using quantitative high-throughput screening. *Environ. Health Perspect.* 116:284-291, 2007

Kavlock RJ, Austin CP, Tice RR. Toxicity Testing in the 21st Century: Implications for Human Health Risk Assessment, *Risk Analysis* DOI: 10.1111/j.1539-6924.2008.01168.x, 2008.

Collins FS, Gray GM, Bucher JR Toxicology. Transforming environmental health protection. *Science* 319:906-907 , 2008.

Dr. Mark J. Hoenerhoff, Staff Scientist, Cellular and Molecular Pathology Branch

Dr. Mark Hoenerhoff recently joined the Cellular and Molecular Pathology Branch at NIEHS as an anatomic pathologist and Investigative Pathology Group Leader. Dr. Hoenerhoff was trained in veterinary medicine at Michigan State University, and spent three years in private practice before returning to MSU to study veterinary pathology. Following his residency in anatomic veterinary pathology, Dr. Hoenerhoff pursued PhD training at the National Cancer Institute at the National Institutes of Health. His research made significant contributions to the field of breast cancer research and stem cell biology.

Dr. Hoenerhoff's major areas of research at the NIEHS include molecular mechanisms of chemically-induced non-neoplastic and neoplastic lesions in rodent models of human disease. His research focuses on genetic mutations and epigenetic alterations resulting from exposure to various environmental contaminants and dietary supplements, leading to the development of neoplastic disease in rodents in NTP carcinogenicity bioassays. By understanding the molecular pathogenesis of cancer, oncogenic events that occur in the rodent as a result of chemical exposure can be related to changes present in the human disease, and conclusions may be made about potential human cancer risk. Another goal of these studies is to distinguish chemical-specific tumor responses from spontaneous events, and to determine if signature mutation patterns that occur in rodents following chemical exposure are similar to patterns relevant to cancer in humans

Selected Publications

Hoenerhoff MJ, Datta S, Bommi P, Sainger R, Guo W, Dimri M, Band H, Band V, Green JE, Dimri GP. Bmi-1 cooperates with H-Ras to transform human mammary epithelial cells via dysregulation of multiple growth regulatory pathways. *Cancer Res*. 67:10286-10295, 2007.

Hoenerhoff MJ, Michalowska AM, Qiu TH, Green JE. Chapter 4: Bioinformatics Approaches to the Analysis of the Transcriptome of Animal Models of Cancer, in Bioinformatics in Cancer and Cancer Therapy, G.J. Gordon, Editor. 2009, Humana Press.

Barkan D, Kleinman H, Simmons JL, Asmussen H, Kamaraju AK, Hoenerhoff MJ, Liu ZY, Costes SV, Cho EH, Lockett S, Khanna C, Chambers AF, Green JE. Inhibition of metastatic outgrowth from single dormant tumor cells by targeting the cytoskeleton. *Cancer Res.* 68:6241-6250, 2008.

Deeb KK, Michalowska AM, Yoon CY, Krummey SM, Hoenerhoff MJ, Kavanaugh C, Li MC, Demayo FJ, Linnoila I, Deng CX, Lee EY, Medina D, Shih JH, Green JE. Identification of an Integrated SV40 T/t-Antigen Cancer Signature in Aggressive Human Breast, Prostate, and Lung Carcinomas with Poor Prognosis. *Cancer Res.* 67:8065-8080, 2007.

Dr. Weichun Huang, Staff Scientist, Biostatistics Branch

Dr. Weichun Huang recently joined the Biostatistics Branch at NIEHS as a staff scientist in Bioinformatics and Biostatistics. Dr. Huang received his PhD degree in Bioinformatics-Statistics from North Carolina State University in 2005 and did his post-doctoral training at Duke University and Boston College. His research has made major

contributions to the following four areas: (1) sequence alignment algorithms for comparative genomics analysis, (2) gene regulation and regulatory DNA motif prediction, (3) conservation and turnover mechanism of transcription factor binding site in mammalian genome, and (4) applications of next-generation sequencing technologies for genetic variation detection.

At the NIEHS, Dr. Huang is focusing on supporting DIR scientists by developing and applying statistical methods and computational tools for large-scale genomics data analysis, particularly, for next-generation sequencing data analysis. The cost-effective next-generation sequencing technologies (e.g., 454, Solexa, and SOLiD) have dramatically sped up genome sequencing/re-sequencing. These new sequencing technologies not only provide a cost-effective approach for generating a deep catalog of human genetic variations, but also present a new and powerful way for studying protein-DNA interaction, gene expression, cancer mutation, genetic and epigenetic gene regulation. The vast amount of new type sequencing data produced by next-generation sequencers, however, pose formidable informatics challenges that are unmet by existing methods and tools. Dr. Huang is interested in developing novel and efficient methods and tools for identifying single-nucleotide polymorphisms (SNP), copy number variations, (CNV), and other large structure variations in the human genome. He is actively involved in the 1000 genomes project for identifying all kinds of genetic variations in the human genome. Dr. Huang is also interested in developing new statistical methods for detecting epigenetic variation with next-generation sequencing data. He is currently collaborating with biologists within and outside the institute for studying CpG methylation pattern and histone modification in the mouse and human genomes, respectively.

Selected Publications

Huang W, Marth GT. EagleView: a genome assembly viewer for next-generation sequencing technologies, *Genome Res.* 18:1538-1543, 2008

Huang W**,** Nevins JR, Ohler U., Phylogenetic simulation of promoter evolution: estimation and modeling of binding site turnover events and assessing their impact on alignment tools, *Genome Biol.* 8:R225, 2007.

Huang W, Umbach, DM Li L. Accurate anchoring alignment of divergent sequences. *Bioinformatics*, 22:29-34, 2006.

Huang W, Umbach DM, Ohler U, Li L. Optimized mixed Markov models for motif identification. *BMC Bioinformatics*, 7**:**279, 2006.

Hillier LW, Marth GT, Quinlan A, Dooling D, Fewell G, Barnett D, Fox P, JGlasscock JI, Hickenbotham M, Huang W, Magrini VJ, Richt RJ, Sander SN, Stewart DA, Stromberg M, Tsung EF, Wylie T, Schedl T, Wilson RK, Mardis ER. Whole Genome Sequencing and Variant Discovery in C. Elegans. *Nat. Methods* 5:183-188, 2008.

Dr. Keith Shockley, Staff Scientist, Biostatistics Branch

Dr. Keith Shockley recently joined the National Toxicology Program as a bioinformatics staff scientist located within the Biostatistics Branch at NIEHS. He was

trained in chemical engineering (Ph.D. 2004, North Carolina State University), where he studied thermal stress response and sugar utilization in hyperthermophilic microorganisms. At NCSU he also investigated the efficacy of continuous culture as a tool to study differential gene expression in microbial systems. Dr. Shockley expanded his interest in bioinformatics within the division of Computational and Systems Biology at The Jackson Laboratory (Bar Harbor, ME). During his postdoctoral training he described PPARγ2-mediated control of stem cell differentiation in mice and uncovered a complex transcriptional architecture in mouse chromosome substitution strains. He also collaborated to explore the molecular basis of sleep in flies and mice.

At the NIEHS, Dr. Shockley is now focusing on supporting NTP research by using genetic and environmental data to improve toxicity testing. As the availability of high-throughput data has increased, a new "systems" approach is emerging in toxicological evaluation. Notably, the Environmental Protection Agency and the National Toxicology Program have recently developed a long-range plan for toxicity testing that involves the testing of large numbers of substances. The goals of this proposal include utilizing the recent advances in molecular toxicology and bioinformatics, increasing reliance on human as opposed to animal data, and improving efficiency in design and costs. Dr. Shockley is interested in developing and applying approaches to aid these objectives. He will assist members of the National Toxicology Program and other agencies to identify genes that control biological responses to environmental exposures, analyze and interpret biological response data from high throughput screening assays, and scrutinize gene expression data from large scale microarray studies. In addition, he will use chemoinformatics to support chemical nominations and biomolecular screening, and build genetic models to predict human toxicity.

Selected Publications

Shockley KR, Lazarenko OP, Czernik PJ, Rosen CJ, Churchill GA, Lecka-Czernik B. PPAR-γ2 nuclear receptor controls multiple regulatory pathways of osteoblast differentiation from marrow mesenchymal stem cells. *J Cell Biochem* (in press).

Shockley KR, Rosen CJ, Churchill GA, Lecka-Czernik B. PPARγ2 regulates a molecular signature of marrow mesenchymal stem cells. ***PPAR Res.*** 2007:81219, 2007

Shockley KR, Churchill GA Gene expression analysis of mouse chromosome substitution strains. ***Mamm. Gen.*** 17:598-614, 2006

Shockley KR, Scott K, Pysz MA, Conners SB, Johnson MR, Montero CI, Wolfinger RD, Kelly RM. Genome-wide transcriptional variation within and between steady states for continuous growth of the hyperthermophile *Thermotoga maritima*. ***Appl. Environ. Microbiol.*** 71:5572-5576, 2005

NIEHS SCIENCE AWARDS DAY

The Sixth Annual DIR NIEHS Science Awards Day was held on November 6, 2008, at the Rall Building on the NIEHS Campus to celebrate the achievements of DIR scientists. The event was open to the public and more than 250 attendees from universities and research institutions in the Triangle Area attended. NIEHS Science Awards Day consisted of 6 oral presentations given by fellows, students, and technicians, 68 poster presentations, oral presentations by the Scientist of the Year, Early Career Award and Outstanding Staff Scientist winners, and an Awards Ceremony. Judging for the awards was done by the NIEHS Board of Scientific Counselors, Extramural Scientists from universities in the Triangle Area, Intramural DIR Scientists and the NIEHS Training Assembly.

The following awards were presented at NIEHS Science Awards Day:

Scientist of the Year: Michael A. Resnick, Ph.D., Laboratory of Molecular Genetics
Early Career Award: Michael B. Fessler, M.D., Laboratory of Respiratory Biology
Outstanding Staff Scientist: Freya Kamel, Ph.D., Epidemiology Branch
Mentor of the Year: Ronald P. Mason, Ph.D., Laboratory of Pharmacology
Best Poster Presentation in Environmental Biology: Stephanie A. Nick McElhinny, Ph.D., Laboratory of Molecular Genetics
Best Poster Presentation in Environmental Diseases and Medicine: Paivi M. Salo, Ph.D., Laboratory of Respiratory Biology
Best Poster Presentation in Environmental Toxicology: Marcelo G. Bonini, Ph.D., Laboratory of Pharmacology
Best Oral Presentation: Daniel A. Gilchrist, Ph.D., Laboratory of Molecular Carcinogenesis
Paper of the Year, From the Laboratory of Molecular Genetics: F. Storici, K. Bebenek, T.A. Kunkel, D.A. Gordenin and M.A. Resnick. "RNA-templated DNA Repair" Nature 447: 338-341, 2007

TRAINING AND MENTORING

The NIH Pathway to Independence Award (K99/R00)

The Pathway to Independence (PI) Award Program is designed to facilitate receiving an R01 award earlier in an investigator's research career. The primary, long-term goal of the PI Award Program is to increase and maintain a strong cohort of new and talented, NIH-supported independent investigators. The PI Award will provide up to five years of support consisting of two phases. The initial phase will provide 1-2 years of mentored support for highly promising, postdoctoral research scientists. This phase will be followed by up to 3 years of independent support contingent on securing an independent research position. Award recipients will be expected to compete successfully for independent R01 support from the NIH during the career transition award period. The PI Award is limited to postdoctoral trainees who propose research relevant to the mission of one or more of the participating NIH Institutes and Centers.

> Arno G. Siraki, Ph.D., received the K99/R00 grant for his proposal entitled, "Mechanisms of aniline-induced agranulocytosis." Dr. Siraki will train in the Laboratory of Pharmacology and Chemistry under the mentorship Dr. Ronald P. Mason.

ST*AR Award from the American Academy of Allergy, Asthma and Immunology

Cindy Visness and Michelle Sever, two graduate students from the Laboratory of Respiratory Biology, received ST*AR Awards from the American Academy of Allergy, Asthma and Immunology. Their mentor is Dr. Darryl Zeldin (Acting Clinical Director, Laboratory of Respiratory Biology).

The North Carolina Society of Toxicology President's Postdoctoral Award for Research

Erik Tokar, Ph.D. was the first place winner for his study entitled "Stem cell selection facilitates arsenic-induced malignant transformation via innate resistance, hyper-adaptability and over-production." His mentor is Dr. Michael Waalkes (Environmental Toxicology Program, NCI at NIEHS).

Scott Auerbach, Ph.D., was the second place winner for his study entitled "Prediction of hepatocarcinogenic potential in male rats using machine learning methods informed by genome-wide expression analysis." His mentor is Dr. Richard Irwin (Toxicology Branch).

TOP DIR PAPERS FOR THE YEAR 2008

Stimulus-Responsive Genes are Marked for Activation

NIEHS investigators found that many genes involved in the *Drosophila* innate immune response and other stimulus-response pathways are poised for activation. These genes recruit the RNA polymerase to the promoter before activation, but the progress of the RNA polymerase into the gene is blocked prior to receipt of an activating signal. In addition to the kinetic advantage afforded by pre-loading the RNA polymerase enzyme on a given gene, a novel function for the RNA polymerase stalled near these gene promoters was uncovered: to block the assembly of repressive chromatin structures. In this way, the presence of a poised RNA polymerase near the promoters of inactive stimulus-responsive genes maintains them in an "activate-able" state, by which the promoter is kept free of nucleosomes and accessible to upstream activators and additional RNA polymerase molecules. These results explain how rapid up-regulation of gene expression occurs in response to specific signals from the environment (e.g. stress and/or immune challenge).

Gilchrist DA, Nechaev S, Lee C, Gosh SKB, Collins J, Li L, Gilmour DS, Adelman K. NELF-mediated stalling of Pol II can enhance gene expression by blocking promoter-proximal nucleosome assembly. *Genes Dev.* 22:1921-1933, 2008.

How Double Helical DNA Is Replicated.

The two DNA strands are oriented anti-parallel to each other yet DNA replication only proceeds in one direction. These two facts require that one DNA strand of the double helix be replicated first by a so-called "leading strand" polymerase, followed slightly thereafter by replication of the other strand by a "lagging strand" polymerase. Amazingly, 54 years after Watson and Crick's description of the DNA double helix, the identity of the polymerases in higher organisms that replicate the leading and lagging strands has remained uncertain. That situation recently changed when, in collaboration with investigators at Washington University in St. Louis, NIEHS scientists published a study indicating that, in the model eukaryote budding yeast, the lagging strand is replicated by DNA polymerase delta. The knowledge that DNA polymerase delta replicates the lagging strand advances our fundamental understanding of how the genome is replicated, and it also places us one step closer to understanding the origins of genome instability that underlie diseases in humans whose occurrence is influenced by the environment.

Nick McElhinny SA, Gordenin DA, Stith CM, Burgers PMJ, Kunkel TA. Division of labor at the eukaryotic replication fork. *Mol. Cell* 30:137-144, 2008.

RNA Recognition Properties of PUF Proteins Can be Adapted by Simple Substitutions

Researchers at the NIEHS determined the three-dimensional atomic structures of a yeast protein, Puf4p, which regulates target messenger RNA stability. These structural studies along with biochemical experiments revealed that the protein binds to its target RNAs with a required 'spacer' nucleotide flipped away from the RNA binding surface. Introduction of two amino acid residue changes reversed the RNA recognition specificity so that the spacer nucleotide is no longer required. Appropriate regulation of target mRNA expression by PUF proteins is critical for maintenance of stem cell maintenance and embryonic development stem cells in humans and other organisms Structural and biochemical studies of yeast PUF4 protein revealed how this family of proteins is adapted to recognize specific, diverse mRNA sequences. This knowledge can be exploited for design of PUF proteins for therapeutic or experimental purposes, such as the development of artificial splicing factors to modulate disease-related defects in pre-mRNA splicing.

Miller MT, Higgin JJ, Hall TMT, Basis of altered RNA-binding specificity by PUF proteins revealed by crystal structures of yeast Puf4p. *Nat. Struct. Mol. Biol.* 14:397-402, 2008.

Structures of DNA Polymerase β Provide the First Glimpse of Pre-Mutagenic DNA Synthesis

Researchers at NIEHS used crystallographic structures of DNA polymerase β (Pol β) with right (matched) and wrong (mismatched) nucleotide substrates to gain insight on how mutations are averted during the enzymatic process of DNA synthesis. The team created G-A and C-A mismatches in the Pol β active site by employing a stable nucleotide analog, dAMPCPP, which could bind to the polymerase but not be inserted. Surprisingly, the structures revealed that both types of substrates (matched and mismatched) produced the same polymerase conformation. However, the mismatched substrate induced a shift in the template strand that produced an abasic site-like pre-synthesis intermediate. The structures are consistent with mutagenesis studies and provide a strategy to avert misinsertion of the wrong nucleotide. This study sheds light on the specific structural changes necessary during high fidelity DNA synthesis, a process central to DNA repair and replication and, ultimately, to protection against mutations due to environmental exposures.

Batra VK, Beard WA, Shock DD, Pedersen LC, Wilson SH. Structures of DNA polymerase beta with active site mismatches suggest a transient abasic site intermediate during misincorporation. *Mol. Cell* 30:315-324, 2008.

Diabetes Risk Associated with Pesticide Use

Pesticide applicators who used chlorinated pesticides on more than 100 days in their lifetime were found to be at greater risk of developing diabetes. NIEHS investigators studied the incidence of diabetes in the Agricultural Health Study, a prospective study of

31,787 licensed pesticide applicators. Since enrollment, 1,171 applicators reported a new diagnosis of diabetes. Among the 50 different pesticides studied, diabetes risk was increased with both ever use and increasing days of use of seven specific pesticides -- aldrin, chlordane, heptachlor, dichlorvos, trichlorfon, alachlor and cynazine. The strongest relationship was found for trichlorfon, with an 85 percent increase in risk for frequent and infrequent users and nearly a 250 percent increase for those who used it more than 10 times. This is one of the largest studies looking at the potential effects of pesticides on diabetes incidence in adults. The results suggest that pesticides may be a contributing factor for diabetes along with known risk factors such as obesity, lack of exercise and having a family history of diabetes. Although the amount of diabetes explained by pesticides is small, these new findings may extend beyond the pesticide applicators in the study. Some of the pesticides used by these workers are used by the general population, though the strength and formulation may vary. Other insecticides in this study are no longer available on the market; however, these chemicals persist in the environment and measurable levels may still be detectable in the general population and in food products.

Montgomery MP, Kamel F, Saldana TM, Alavanja MCR, Sandler DP. Incident diabetes and pesticide exposure among licensed pesticide applicators: Agricultural Health Study 1993 – 2003. *Am. J. Epidemiol*. 167:1235-1246, 2008.

An expanded biological repertoire for Inositol(3,4,5,6)-tetraphosphate through its modulation of ClC-3 function.

Inositol phosphates are “second messengers” that can play key roles in helping cells adapt to environmental insults, toxins, infections, or genetic defects. Inositol(3,4,5,6)-tetraphosphate (Ins(3,4,5,6)P(4)) inhibits plasma membrane chloride ion flux in secretory epithelia. However, in most other mammalian cells, receptor-dependent elevation of Ins(3,4,5,6)P(4) levels is an "orphan" response that lacks biological significance. NIEHS scientists have shown that the chloride ion channel, ClC-3, is inhibited by Ins(3,4,5,6)P4, thus defining a signal transduction pathway involving Ins(3,4,5,6)P4. They have also expanded the range of cell types that respond to Ins(3,4,5,6)P4 by showing that Ins(3,4,5,6)P(4) inhibits the ClC-3 conductance in postsynaptic membranes of neonatal hippocampal neurons. This signal transduction pathway could be involved in other cellular processes in which ClC-3 function may be regulated by Ins(3,4,5,6)P4 including tumor cell migration, apoptosis, and inflammatory responses, suggesting that Ins(3,4,5,6)P4 is a ubiquitous cellular signal with diverse biological actions.

Mitchell J, Wang X, Zhang G, Gentzsch M, Nelson DJ, Shears SB. An Expanded Biological Repertoire for Ins(3,4,5,6)P4 through its Modulation of ClC-3 Function *Curr. Biol.* 18:1600-1605, 2008.

DEPs Involved in a Novel Blood-Brain Barrier Signaling Pathway

Scientists from NIEHS have shown that diesel exhaust particles alter blood-brain barrier function through oxidative stress and proinflammatory cytokine production. Diesel exhaust particles are the main particulate component of urban air pollution worldwide. When brain capillaries isolated from rats are exposed to diesel exhaust particles, a signaling pathway involving NADPH oxidase and tumor necrosis factor alpha was activated, resulting in increased expression of P-glycoprotein, a major blood-brain barrier transporter. The results reveal a novel blood-brain barrier signaling pathway activated by urban air pollutants that could affect pharmacotherapy for a number of CNS diseases.

Hartz AM, Bauer B, Block ML, Hong JS, Miller DS. Diesel exhaust particles induce oxidative stress, proinflammatory signaling, and P-glycoprotein up-regulation at the blood-brain barrier. *FASEB J.* 22: 2723-2733, 2008

Neuronal Activity Reshapes Brain Circuitry

During postnatal development, connections between neurons, or synapses, are formed in abundance and then eliminated to shape the brain circuitry according to experience. NIEHS researchers discovered that continued weakening of synapses, induced with prolonged low-frequency stimulation, can lead to loss of synapses. Small synapses were found to be most susceptible to loss. This finding represents the first step in uncovering the mechanisms responsible for such activity-dependent synapse elimination, which likely plays an important role in developmental disorders such as schizophrenia and autism.

Bastrikova N, Gardner GA, Reece JM, Jeromin A, Dudek SM. Synapse elimination accompanies functional plasticity in hippocampal neurons. *Proc. Natl. Acad. Sci. USA.* 105:3123-3127, 2008

The Human ERG1 Channel Polymorphism, K897T, Creates a Phosphorylation Site That Inhibits Channel Activity

Polymorphisms in the human ether-a-go-go-related gene 1, hERG1, are associated with cardiac arrhythmias. The Kv11.1 channels encoded by hERG1 are also essential for rhythmic excitability of the pituitary, where they are regulated by thyroid hormone through a signal transduction cascade involving the phosphatidylinositol 3-kinase (PI3K) and the Ser/Thr-directed protein phosphatase, PP5. NIEHS investigators showed that the hERG1 polymorphism at codon 897, which is read as a Thr instead of a Lys, creates a new phosphorylation site for the Akt protein kinase on the Kv11.1 channel protein. Consequently hormonal signaling through the PI3K signaling cascade, which normally stimulates the K897 channels through PP5-mediated dephosphorylation, inhibits the T897 channels through Akt-mediated phosphorylation. Thus, hormonal regulation of Kv11.1 in humans with the K897T polymorphism is predicted to prolong the QT interval of cardiac myocytes. A systematic bioinformatics search for single nucleotide polymorphisms in human ion channel genes identified fifteen additional candidates for such "phosphorylopathies," which are predicted to create or destroy putative phosphorylation sites. Thus, changes in protein phosphorylation might represent a general mechanism for the effects of genetic variation on human health and its interaction with the environment.

Gentile S, Martin N, Scappini E, Williams J, Erxleben C, Armstrong DL. The human ERG1 channel polymorphism, K897T, creates a phosphorylation site that inhibits channel activity. *Proc. Natl. Acad. Sci. USA.* 105:14704-14708, 2008.

NOS and Nitroglycerin-Mediated Vasodilation

Nitroglycerin helps patients with angina and a past history of heart attacks by relaxing the smooth muscles around blood vessels, allowing more blood to reach cardiac muscles, but the exact mechanism involved in nitric oxide synthase (NOS) activation was unknown. Researchers at NIEHS and the University of Sao Paulo School of Medicine have found evidence that nitroglycerin triggered constitutive NOS activation using cell cultures, isolated vessels, and whole animals. The work may offer insight into the molecular mechanisms involved in nitrate resistance. The team's studies indicated that endothelial NOS was phosphorylated at Ser1177 on the endothelial isoform and Ser852 on the neuronal isoform in the aortae of mice and rats treated with nitroglycerin, which confirmed that isoforms of NOS were involved in vasorelaxation. Aortic ring studies determined that high doses of nitroglycerin produced vasodilation that was independent of the endothelium and could not be annulled by NOS inhibitors. At higher doses nitroglycerin is known to be bioactivated to nitric oxide.

Bonini MG, Stadler K, Silva Sde O, Corbett J, Dore M, Petranka J, Fernandes DC, Tanaka LY, Duma D, Laurindo FR, Mason RP. Constitutive nitric oxide synthase activation is a significant route for nitroglycerin-mediated vasodilation. *Proc. Natl. Acad. Sci. USA.* 105:8569-8574, 2008.

AWARDS AND HONORS

Dr. Trevor K. Archer (Chief, Laboratory of Molecular Carcinogenesis) served on the Editorial Board of the *Journal of Biological Chemistry*.

Dr. Donna Baird (Epidemiology Branch) was the Raymond Pearl Memorial Lecturer at the 2008 annual meeting of the Human Biology Association and was named Associate Editor of the *American Journal of Epidemiology.*

Dr. Jack Bishop (Toxicology Branch) received the Environmental Mutagen Society Appreciation Award for Exemplary and Dedicated Service to the Society as Treasurer.

Dr. John Cidlowski (Chief, Laboratory of Signal Transduction) received the Edwin B. Astwood Award from the Endocrine Society in 2008.

Dr. William Copeland (Laboratory of Molecular Genetics) was appointed to the Editorial Board of the *Journal of Biological Chemistry.*

Dr. Greg Dinse (Biostatistics Branch) was appointed to the Editorial Board of the journal *Lifetime Data Analysis.*

Dr. E. Mitch Eddy (Laboratory of Reproductive and Developmental Toxicology) served as Associate Editor of *Biology of Reproduction*; was on the Executive Council of The Society for the Study of Reproduction and; was the Chair of the North American Testis Workshop.

Dr. Dori Germolec (Toxicology Branch) was elected to serve on the Education Committee for the Society of Toxicology.

Dr. Joyce Goldstein (Laboratory of Pharmacology) served on the Editorial Boards of *Drug Metabolism and Deposition* and *Drug Metabolism Reviews.*

Dr. Dmitry Gordenin (Laboratory of Molecular Genetics) served on the Editorial Board of *Mutation Research, Fundamental and Molecular Mechanisms of Mutagenesis*.

Dr. Traci Hall (Laboratory of Structural Biology) was named to the American Society for Biochemistry and Molecular Biology Meetings Oversight Committee.

Dr. Anton Jetten (Laboratory of Respiratory Biology) served on the Editorial Boards of *Molecular and Cellular Biology*, the *Journal of Biomedicine and Biotechnology* and the *International Journal of Cell Biology*.

Dr. Maria B. Kadiiska (Laboratory of Pharmacology) received the "Free Radical Biology & Medicine Top most cited papers 2005 - 2007 Award" from Elsevier Publishers at the 15th Annual Meeting of the Society for Free Radical Biology and Medicine for her paper "Biomarkers of Oxidative Stress Study II. Are oxidation products of lipids, proteins, and DNA markers of CCl4 poisoning?" *Free Radic Biol Med* 38: 711-718, 2005.

Dr. Steven Kleeberger (Chief, Laboratory of Respiratory Biology) was the keynote speaker at the Society of Toxicology Symposium "Host susceptibility and chemical safety testing: new approaches to estimate risks in the human population" and at the Gordon Conference on "Mechanisms of Toxicity". Dr. Kleeberger also served on the EPA Scientific Advisory Board on Particulate Matter (PM) Research Centers Program as well as a panelist on the EPA Ozone National Ambient Air Quality Standards Review Workshop.

Dr. Thomas Kunkel (Laboratory of Molecular Genetics; Chief Laboratory of Structural Biology) was the Keynote Speaker at the Workshop on AID Biology and Its Role

in Human Disease and was the Distinguished "Beach Lecturer" at Perdue University.

Dr. Frederick W. Miller (Office of Clinical Research) was elected to the Editorial Board of *The Open Rheumatology Journal.*

Dr. Pierre Bushel (Biostatistics Branch) was awarded a Yerby fellowship as an Assistant Professor of Bioinformatics at the Harvard School of Public Health, Harvard University with dual appointments in the Department of Biostatistics and Department of Environmental Health.

Dr. David Resnik (Office of the Scientific Director) served as Book Review Editor for *Policy Studies in Ethics, Law, and Technology* and was on the Editorial Boards of *The Open Clinical Trails Journal* and *Environmental Health Insights.*

Dr. Lisa Rider (Office of Clinical Research) was invited to serve on the Editorial Board of *The Open Rheumatology Journal.*

Dr. Robert Sills (Chief, Cellular and Molecular Pathology Branch) served as the Associate Editor of the Environmental Pathobiology Section of *Veterinary Pathology*.

Dr. William Stokes (National Toxicology Program Operation Branch) received the 2008 James A. McCallam Award from the Association of Military Surgeons; the Karl F. Meyer-James H. Steele Gold Head Cane Award from the American Veterinary Medical Association and; the Field Medical Readiness Badge from the U.S. Public Health Service.

Dr. Nigel Walker (National Toxicology Program Operation Branch) was appointed to the Editorial Boards of *Environmental Health Perspectives* and *Toxicology and Applied Pharmacology*.

Dr. Allen Wilcox (Epidemiology Branch) received an honorary doctorate from the University of Bergen, Norway.

Dr. Samuel Wilson (Deputy Director and Laboratory of Structural Biology) was elected a fellow of the American Association for the Advancement of Science.

Dr. Jerrel Yakel (Laboratory of Neurobiology) was elected a fellow of the American Association for the Advancement of Science.

Dr. Darryl Zeldin (Acting Clinical Director, Laboratory of Respiratory Biology) served on the Editorial Boards of the *Journal of Biological Chemistry,* the *American Journal of Physiology: Lung Cellular and Molecular Biology,* the *Journal of Allergy and Clinical Immunology, Prostaglandins and Other Lipid Mediators, The Open Environmental Journal, and Molecular and Cellular Pharmacology.*

UPDATE
National Toxicology Program

JANUARY 2009

Headquartered at the
National Institute of Environmental
Health Sciences NIH-HHS

Linda S. Birnbaum to Lead NIEHS and NTP

On December 3, Dr. Raynard S. Kington, acting director of the National Institutes of Health, announced the appointment of Linda S. Birnbaum, Ph.D., D.A.B.T., A.T.S., as director of the NIEHS and NTP. Dr. Birnbaum is currently a senior advisor at the EPA, where she served for 16 years as director of the Experimental Toxicology Division. She will begin her appointment in mid January 2009.

Humane Society and Procter and Gamble Recognize NTP for Advancing Alternatives to Animal Testing

Article by Robin Mackar, reprinted from *eFACTOR*, January 2009

On December 18, the Humane Society of the United States (HSUS) and Procter and Gamble presented Ray Tice, Ph.D., of the National Toxicology Program (NTP) an award for the outstanding scientific contributions that he and others are making to advance viable alternatives to animal testing.

The North American Alternative Awards were presented at HSUS Washington office by the executive vice president of the HSUS, Andrew Rowan, Ph.D., and Len Sauers, Ph.D., vice president of product safety, regulatory and technical relations for Procter and Gamble. The awards recognize the efforts of the recipients to work toward the elimination of animal testing for consumer product safety while ensuring safe products for consumers and the environment.

Raymond Tice, Ph.D., chief of the NTP Biomolecular Screening Branch and deputy director of the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods, was joined by colleagues Christopher Austin, M.D., of the National Human Genome Research Institute (NHGRI) and Robert Kavlock, Ph.D., of the Environmental Protection Agency (EPA) to receive the award. The award includes a $25,000 grant to support the ongoing alternative methodologies efforts.

The three agencies signed a Memorandum of Understanding (MOU) in February 2008 to use the NIH Chemical Genomics Center's (NCGC) high-speed, automated screening robots to test suspected toxic compounds using cells and isolated molecular targets instead of laboratory animals. The award will be used to develop toxicity signatures that help determine how toxic a chemical might be and what type of toxicity it might cause.

"I am pleased that we are receiving recognition by our stakeholders for our efforts," said Tice. "The NTP and our sister agencies are working hard to implement the vision set out by the National Research Council's 2007 Report, Toxicity Testing in the 21st Century: A Vision and a Strategy."

NTP Unveils New Non-Cancer Study Criteria

Article by Eddy Ball, reprinted from *eFACTOR*, January 2009

The National Toxicology Program (NTP) is trying to bring the same rigorous standards it uses for classifying the outcomes of its cancer studies to many of its non-cancer studies, according to presentations made by speakers at the NTP Board of Scientific Counselors (BSC) meeting November 20 in Rodbell Auditorium. The Board voted to accept three working group reports addressing the establishment of new criteria for future NTP immunotoxicology, reproductive and developmental studies.

The three sets of criteria were presented by BSC Criteria Working Group (CWG) chairs Nancy Kerkvliet, Ph.D., who chaired the immunotoxicology group, and Edward Carney, Ph.D., who chaired the reproductive and developmental groups. The criteria are similar to those used with the agency's gold-standard cancer studies, which are based on five levels of evidence ranging from clear evidence to no evidence and inadequate study.

Toxicology Branch Acting Chief and reproduction and development discipline leader Paul Foster, Ph.D., opened the discussion by explaining why NTP decided to establish the strength of evidence criteria. "We've had a goal now for the best part of 18 months to employ the same rigorous standards used historically to review our carcinogenicity bioassays with the NTP non-cancer studies," he said. He also noted that the NTP did not undertake this effort in isolation and emphasized the critical role the working groups played in helping establish the criteria for the various studies. The working groups, made up of representatives from government, industry and academia, met in late summer 2008.

"We have a desire to have uniform [non-cancer] criteria for chemicals across studies and for studies across chemicals, much as we have for the cancer bioassays," Foster continued, "so that the Board, the NTP staff and the public can have some kind of consistency in the ways these findings are reported."

Foster and Toxicology Branch immunology discipline leader Dori Germolec, Ph.D., expressed their confidence that the new criteria will give NTP non-cancer studies the same rigor, consistency and authority that NTP cancer reports have enjoyed for decades. The criteria, they maintained, will increase the utility of the non-cancer studies for regulatory agencies by clarifying the official government opinion of the hazards posed by chemicals.

Following presentations by the chairs of the three CWGs, Board members engaged in a lively discussion before giving NTP the go-ahead to progress to the next phase of finalizing the criteria. NTP scientists agreed to address Board concerns about terminology that might lead to misinterpretation by those not as familiar with toxicology.

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Upcoming Events

February 24, 2009

NTP Board of Scientific Counselors Meeting

NIEHS, 111 TW Alexander Dr.
Research Triangle Park, NC

February 25, 2009

NTP Board of Scientific Counselors Technical Reports Review Subcommittee Meeting

NIEHS, 111 TW Alexander Dr.
Research Triangle Park, NC

June 25-26, 2009

Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) Meeting

Hilton Arlington
950 North Stafford Street
Arlington, VA

http://ntp.niehs.nih.gov/go/calendar

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In the course of the Board's discussion, Foster, Germolec and NTP Associate Director John Bucher, Ph.D., emphasized that the non-cancer studies will be clearly presented as hazard studies with multiple interrelated end points and not as risk assessments, which require exposure data along with consideration of hazards. The levels of evidence, they assured the Board, will be noted as applying under the conditions of the individual study in regard to specific sexes of specific species for the particular studies.

All CWGs proposed four levels of evidence: clear evidence, some evidence, equivocal evidence and no evidence. The reproductive and developmental toxicity CWG also included the category "inadequate study" for studies with qualitative or quantitative limitations that could not be interpreted for toxicity — a category that will also be incorporated into the final immunotoxicology criteria.

Timeline for Non-Cancer Criteria

According to Foster and Germolec, revisions to the levels of evidence statements for the three sets of criteria incorporating the Board's recommendations should be completed by the end of January 2009.

The proposed criteria are slated for formal presentation to attendees at the Society for Toxicology (SOT) 48th Annual Meeting and ToxExpo March 15-19 in Baltimore, MD by Foster and Germolec.

Germolec expects to begin applying the immunotoxicology criteria to studies for peer review by the end of 2009. Foster said that the first reproductive and developmental studies featuring the new criteria could appear as early as early as 2010.

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NTP Staff Honored

William Stokes Honored

Rear Admiral William Stokes, Director of NICEATM, received the James A. McCallam Award at the 114th meeting of the Association of Military Surgeons (AMSUS) of the United States in San Antonio, TX on November 12, 2008. RADM Stokes received the award in recognition of his outstanding accomplishments in the field of medicine and health. RADM Steven Galson, Acting Surgeon General of the United States, and Major General (ret) George Anderson, AMSUS Executive Director presented the award.

RADM Stokes was also honored with the Karl F. Meyer-James H. Steele Gold Head Cane Award by the American Veterinary Medical Association (AVMA). RADM Stokes received the award in recognition of significant career achievements that have advanced human health through the practice of veterinary epidemiology and public health. Dr. Gregory Hammer, the 2007-08 President of the AVMA, presented the award at the 145th AVMA Annual Convention in New Orleans on July 22, 2008.

Scott Auerbach Wins NC SOT Award

Dr. Scott Auerbach, a postdoctoral fellow in the Toxicology Branch, received second place in the President's Award for Research Competition at the October annual meeting of the NC Society of Toxicology (SOT) for the study titled "Prediction of hepatocarcinogenic potential in male rats using machine learning methods informed by genome-wide expression analysis." His mentor and collaborator on the research is Dr. Rick Irwin.

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Directors Annual Awards Ceremony

The NIEHS honored employees at the 2008 Director's Annual Honor Awards Ceremony on December 18. Several NTP staff received Merit Awards, which is the highest honor award an Institute Director can approve. It recognizes contributions in the areas of leadership, significant scientific research or administrative support, creativity, and notable competence or administrative management of the institute.

Joseph Roycroft, Ph.D. and Molly Vallant *for significant and sustained contributions to the high quality of studies conducted for the National Toxicology Program.*

John Bucher, Ph.D., Paul Foster, Ph.D., Denise Lasko, Michael Shelby, Ph.D., Diane Spencer, M.S., Kristina Thayer, Ph.D., and Mary Wolfe, Ph.D., in a group award with Robin Mackar and Allen Dearry, Ph.D. *for exemplary service in facilitating and organizing the evaluation of the bisphenol A report*.

Paul Foster, Ph.D., John French, Ph.D., Robert Sills, Ph.D., Cynthia Smith, Ph.D., Raymond Tice, Ph.D., Nigel Walker, Ph.D., and Mary Wolfe, Ph.D., *for significant scientific and technical contributions to the implementation of the realignment of the National Toxicology Program*.

Dori Germolec, Ph.D., Grace Kissling, Ph.D., and Sharon Soward, received special recognition as recipients of the NIEHS Unsung Hero Award. This award recognizes individuals *for behind the scenes contributions that keep the NIEHS operating in harmony.*

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NTP at SOT

Plan to stop by booth #1673 and visit NTP at the Society of Toxicology (SOT) 48th Annual Meeting and ToxExpo March 15-19, 2009, in Baltimore, MD. NIEHS and its journal EHP will be adjacent to NTP in booth #1772.

NTP to Unveil New Non-Cancer Evaluation Criteria at SOT

The NTP is working to bring the same rigorous standards it uses for classifying the outcomes of its cancer studies to many of its non-cancer studies (see related story, page 2). On March 17, 2009, from 1:30-2:30 PM in Room 337, the NTP will sponsor a session to discuss the establishment of its new evaluation criteria for future NTP immunotoxicology, reproductive and developmental studies and how these criteria can be used to draw study conclusions. The NTP invites you to join them for the exhibitor-hosted session to hear about the new evaluation criteria.

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NTP Board of Scientific Counselors

The NTP Board of Scientific Counselors (BSC) will meet on February 24, 2009, at the NIEHS, 111 TW Alexander Drive, Research Triangle Park, NC. The primary agenda item is the public peer review by the BSC of draft substance profiles for five candidate substances (aristolochic acids, captafol *ortho*-nitrotoluene, riddelliine and styrene) under consideration for the 12th Report on Carcinogens.

This meeting was announced in the Federal Register on December 22 (73 FR 78365) and materials for the meeting, including the draft substance profiles, are posted on the NTP website (http://ntp.niehs.nih.gov/go/165) or can be obtained by contacting Dr. Barbara Shane (contact information below). This meeting is open to the public and public comment, both written and oral, is welcome on any draft profile.

Contact Information: Dr. Barbara Shane, Executive Secretary, NTP Office of Liaison, Policy and Review, NIH/NIEHS, P.O. Box 12233, Research Triangle Park, NC 27709; T: (919) 541-4253; FAX: (919) 541-0295; shane@niehs.nih.gov

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NTP Board of Scientific Counselors Technical Reports Review Subcommittee

The Subcommittee is scheduled to meet on February 25, 2009, at the NIEHS, 111 TW Alexander Drive, Research Triangle Park, NC to peer review the findings and conclusions from 6 draft NTP Technical Reports on studies conducted in conventional rats and mice.

The draft reports tentatively scheduled for review are:

TR 557	β-Myrcene	TR 560	Androstenedione
TR 558	3,3',4,4'-Tetrachloroazobenzene	TR 561	Tetralin
TR 559	2,3',4,4',5- Pentachlorobiphenyl (PCB 118)	TR 562	Goldenseal root powder

Information about the meeting was announced in the Federal Register on December 18 (73 FR 77026) and materials for the meeting are posted on the NTP website (http://ntp.niehs.nih.gov/go/15833) or can be obtained by contacting Dr. Barbara Shane (contact information below). Draft technical reports will be available by January 14, 2009. This meeting is open to the public, and public comment, both written and oral, is welcome on any draft report.

Contact Information: Dr. Barbara Shane, Executive Secretary, NTP Office of Liaison, Policy and Review, NIH/NIEHS, P.O. Box 12233, Research Triangle Park, NC 27709; T: (919) 541-4253; FAX: (919) 541-0295; shane@niehs.nih.gov

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Report on Carcinogens (RoC)

Cobalt-Tungsten Carbide Powders and Hard Metals

The public meeting of the RoC Expert Panel on Cobalt-Tungsten Carbide Powders and Hard Metals took place on December 9-10, 2008, at the Sheraton Chapel Hill Hotel, Chapel Hill, NC. The expert panel peer-reviewed the draft background document on cobalt-tungsten carbide powders and hard metals and made a recommendation on its listing status in the 12th RoC. The expert panel recommended that cobalt-tungsten carbide powders and hard metals be listed as *reasonably anticipated to be a human carcinogen* based on limited evidence of carcinogenicity in humans and supporting mechanistic data. The NTP plans to have the expert panel's recommendation on listing status and scientific justification (Expert Panel Report, Part B) posted on the RoC website (http://ntp.niehs.nih.gov/go/29682) and available for public comment by late January 2009. The final background document on cobalt tungsten carbide powders and hard metals should be posted on the RoC website in February.

Contact Information: Dr. Ruth M. Lunn, Report on Carcinogens Office, NIH/NIEHS, P.O. Box 12233, Research Triangle Park, NC 27709; T: (919) 316-4637; FAX: (919) 541-0144; lunn@niehs.nih.gov

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NTP Center for the Evaluation of Risks to Human Reproduction (CERHR)

Updated Evaluations of Genistein and Soy Formula Planned

In 2006, CERHR initiated the evaluations of genistein and soy formula. An expert panel meeting was held in March 2006, and the final expert panel reports for both substances were released in May 2006. Draft NTP briefs, which provided the NTP's conclusions regarding the potential for genistein or soy formula to adversely affect reproduction and/or development in exposed humans, were released for public comment and peer review in November 2006. CERHR has not finalized these evaluations, finalized the briefs, or issued the NTP-CERHR monographs on these substances. Since 2006, a substantial number of new studies related to human exposure or reproductive or developmental toxicity have been published and CERHR has determined that updated evaluations of genistein and soy formula are needed. Plans are underway to convene a second expert panel to consider this new literature and to review and update the conclusions drawn by the previous panel.

A Federal Register notice (http://ntp.niehs.nih.gov/files/73_FR_192_Updt_Evals_508.pdf) was published on October 2, 2008, requesting public comment on the proposed review as well as nominations of expert panel members. As plans for these evaluations are finalized, they will be announced in the Federal Register and this newsletter.

Contact Information: Dr. Michael D. Shelby, Director CERHR, NIH/NIEHS, P.O. Box 12233, Research Triangle Park, NC 27709; T: (919) 541-3455; FAX: (919) 316-4511; shelby@niehs.nih.gov

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Educational Opportunities in Pathology

Rodent Pathology Course

NTP staff from the Cellular and Molecular Pathology Branch including Drs. Angela King-Herbert, David Malarkey, Susan Elmore, and Ron Herbert recently served on the organizing committee for the Fourth RTP Rodent Pathology Course on Immunopathology held September 14-16, 2008. Dr. Susan Elmore spoke on "Structure and Function of the Immune System" and Ms. Julie Foley, also from CMPB, presented timely information on "FAQs regarding the Collection and Fixation of Tissue for Immune System Regulation." The course series, initially conceived by Drs. Robert Maronpot and Jeff Everitt, began in 2002 and is designed to provide useful information on current issues and techniques in rodent pathology to research and diagnostic pathologists, pathologists-in-training, and interested members of the research community. Past courses have covered reproductive pathology, neurological pathology, and cardiopulmonary pathology. To learn more about this continuing education series go to http://continuingeducation.ncsu.edu/rodentpath/.

NTP Satellite Symposium

The 10th Annual NTP Satellite Symposium will be held on June 20, 2009, in conjunction with the Society of Toxicologic Pathology (STP) 28th Annual Meeting in Washington, DC. This all-day pathology symposium is designed to provide continuing education to the toxicological pathology community using an interactive approach to diagnostic

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histopathology. This year's topic is tumor pathology, which complements the STP annual meeting's theme on cancer. Case studies will be presented and 100 audience members will have an opportunity to vote anonymously on the diagnosis for each case using wireless keypads; the fun begins when the voting results are displayed to everyone for general discussion. Dr. Susan Elmore from the NTP Cellular and Molecular Pathology Branch (elmore@niehs.nih.gov) is the symposium chair. It is a free event, but due to space limitations registration is required. To learn more and register for the symposium, go to http://www.toxpath.org/AM2009/gen.asp.

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NTP Interagency Center for the Evaluation of Alternative Toxicological Methods NICEATM)

ICCVAM Issues Recommendations on *In Vitro* Pyrogenicity Test Methods

NICEATM announces availability of the (1) *ICCVAM Test Method Evaluation Report: Validation Status of Five* In Vitro *Test Methods Proposed for Assessing Potential Pyrogenicity of Pharmaceuticals and Other Products* (NIH Publication Number 08-6392) and (2) *Final Background Review Document: Validation Status of Five* In Vitro *Test Methods Proposed for Assessing Potential Pyrogenicity of Pharmaceuticals and Other Products* (NIH Publication Number 08-6391). The evaluation report provides recommendations from the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) on the usefulness and limitations of five *in vitro* pyrogen test methods for detecting Gram-negative bacterial endotoxin in human parenteral pharmaceuticals. The recommendations are based on ICCVAM's comprehensive review of the scientific validity of the methods that included an independent scientific peer review by an international expert panel. The report also provides recommended test method protocols for the five methods and recommendations for future studies that might broaden the usefulness of the test methods.

Endotoxin is a component of the Gram-negative bacterial cell membrane that can induce fever (i.e., is pyrogenic). Parenteral pharmaceuticals, fluids for injection, medical devices, and human biological products must be properly and accurately evaluated for the presence of endotoxin contamination prior to their release for clinical use.

ICCVAM recommends that the test methods should be considered for use on a case-by-case basis to detect Gram-negative endotoxin in human parenteral drugs, subject to product-specific validation to demonstrate equivalence to the rabbit pyrogen test, in accordance with applicable U.S. Food and Drug Administration regulations. When determined to be valid for specific products and used in this manner, these methods can reduce the number of animals needed for pyrogenicity testing. ICCVAM also recommends that these and other *in vitro* alternative test methods should be considered prior to *in vivo* pyrogenicity testing, and should be used where determined appropriate for a specific testing situation. However, ICCVAM concludes that none of these test methods can be considered as a complete replacement for the rabbit pyrogen test for all testing situations for detecting Gram-negative endotoxin.

The final background review document provides the data and analyses that support the current validation status of these five *in vitro* test methods. Availability of the test method evaluation report and background review document was announced on November 24, 2008, in the Federal Register (73 FR 71003) and are available on the NICEATM/ICCVAM web site (http://iccvam.niehs.nih.gov/methods/pyrogen/pyrogen.htm). The European Centre

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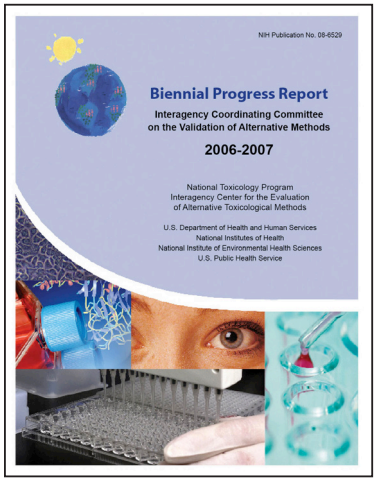
for the Validation of Alternative Methods submitted the five *in vitro* pyrogen test methods to ICCVAM for formal evaluation of their scientific validity for regulatory testing purposes.

The ICCVAM recommendations have been forwarded to U.S. Federal agencies for consideration of regulatory acceptance according to their specific statutory requirements. The deadline for the agencies' responses is April 22, 2009; the responses will be posted on the NICEATM-ICCVAM website.

2006-2007 ICCVAM Biennial Report



The Biennial Progress Report for the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) for 2006-2007 was released on October 23, 2008 (73 FR 63150). The biennial report describes major activities over the past two years and reiterates ongoing efforts by NICEATM and ICCVAM to promote the development, validation, and regulatory acceptance of new test methods that will reduce, refine, and replace the use of animals in testing while maintaining and promoting scientific quality and the protection of people, animals, and the environment. Selected highlights include:

- ICCVAM recommended to Federal agencies the first non-animal, ocular, safety-testing methods that can identify substances causing severe eye damage, such as blindness.
- ICCVAM determined that two non-animal, cell-based assays could reduce animal use for testing that is required to determine if chemicals and products can cause acute poisoning, the most common product safety test performed.
- ICCVAM completed evaluation of five non-animal test methods for assessing the fever inducing, or pyrogenicity, potential of injectable pharmaceuticals and other products.
- NICEATM initiated an international validation study of a cell-based test method to determine if it can identify substances that may disrupt normal hormonal function.
- NICEATM and ICCVAM strengthened collaborations with European and Japanese counterparts in the areas of validation studies and review activities.

Since its establishment in 1997, ICCVAM has contributed to the approval or endorsement of 18 alternative safety-testing methods by Federal regulatory agencies. These test methods have significantly reduced animal use and improved animal welfare. ICCVAM has also identified critical research, development, and validation efforts needed to further advance numerous other alternative methods.

The biennial report is available on the NICEATM-ICCVAM website (http://iccvam.niehs.nih.gov/).

Update on the Murine Local Lymph Node Assay (LLNA)

NICEATM has received and is reviewing additional data and information on three non-radioactive LLNA test methods and formulation data from over 70 traditional LLNA studies. These data will be used in an updated evaluation of the usefulness and limitations of the LLNA test methods. In addition, previous analyses performed to evaluate the use of the LLNA for predicting skin sensitization potency in humans have been updated to include new human reference data. An independent peer review panel is scheduled to meet in public session on April 28-29, 2009, to consider draft ICCVAM test method recommendations on the updated LLNA test method analyses.

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NIEHS Scientists Shine at Research Festival

Article by Eddy Ball, reprinted from *eFACTOR*, November 2008

NIEHS and National Toxicology Program (NTP) scientists were among the thousands of people attending the 21st annual NIH Research Festival October 14-17 at the Masur Auditorium and Natcher Conference Center on the NIH campus in Bethesda, MD. The event included a plenary session on obesity, 18 concurrent symposia sessions, poster sessions with more than 500 entries, a Fellows Award for Research Excellence (FARE) program and award ceremony, a symposium and career fair for postdocs, and special exhibits spread over the three days.

Representing NIEHS on the program were three senior investigators presenting at a symposia on "Genetic Susceptibility — The Link between Environmental Exposure and Human Disease," chaired by NTP Acting Chief and Staff Scientist in the Host Susceptibility Branch Jef French, Ph.D. Seven NIEHS postdoctoral fellows also made the trek to Bethesda, six of them to participate in the poster competition (see text box). An additional postdoctoral fellow did not attend the festival although his research was judged as part of the poster presentation.

In addition to serving as chair for the symposia, French made a presentation on analyzing DNA strand break repair and susceptibility to tumor suppressor gene loss associated with loss of heterozygosity in response to human carcinogen exposure. He was joined by NIEHS Senior Investigator and Chief of the Laboratory of Respiratory Biology Steve Kleeberger, Ph.D., and NTP Toxicology Branch Staff Scientist June Dunnick, Ph.D., who also spoke at the session.

In his presentation, Kleeberger described his work in identifying the transcription factor NRF2 as a critical determinant of susceptibility to hyperoxic lung injury. Dunnick's presentation explored how environmental factors may contribute to cardiac disease and how the NIEHS plans to use mouse models to identify highly penetrant allelic variants of genes that modify or influence cardiotoxicity in order to determine orthologous human genes. Two National Cancer Institute investigators, Kent Hunter, Ph.D. and Karlyne Reilly, Ph.D., also presented at the symposium.

One of the young scientists from NIEHS, Visiting Fellow Wataru Nakai, Ph.D., of the Chromosome Stability Group headed by Principal Investigator Mike Resnick, Ph.D., won a FARE Award for his research. His submission, "Transition of a Double-Strand Break to a Chromosome Break is Efficiently Prevented by RMX, Exonuclease I and MCD1," was part of the Genetics/Genomics Poster Session on October 15.

NIEHS Postdoctoral Fellow Jennifer Adair served as a member of the FARE Committee for the Research Festival.

NIEHS Postdocs at the NIH Research Festival

The annual FARE competition, now in its 14th year, selects the top twenty-five percent of abstracts from fifty different study sections to receive a $1,000 travel award. In addition to Visiting Fellow Wataru Nakai, Ph.D., six other NIEHS fellows presented their work in the competition:

Scott Auerbach, Ph.D., in the Cancer session

Yin Li, Ph.D. in the Cell Biology session

Yang Cao, Ph.D., in the Epidemiology session

Xueqian (Shirley) Wang, Ph.D., in the Imaging session

Jianxin Shen, Ph.D., in the Neurobiology and Behavior session

Saurabh Chatterjee, Ph.D., in the Oxidative Stress session (in absentia)

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NTP Publications July-September 2008

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To subscribe to the listserv and receive the NTP Update as well as other NTP news and announcements electronically, register online at http://ntp.niehs.nih.gov or send e-mail to ntpmail-request@list.niehs.nih.gov with the word "subscribe" as the body of the message or contact Central Data Management. Additional information about the NTP along with announcements of meetings, publications, study results and its centers is available on the Internet at http://ntp.niehs.nih.gov.

The NTP website offers electronic files of the Report on Carcinogens and the library of NTP Technical Reports and NTP Toxicity Reports. The PDF files of these reports are available free-of-charge through the NTP website at http://ntp.niehs.nih.gov (see Resources).

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FEATURED ACTIVITIES of DERT
February 2009

MEETINGS

Genes, Environment and Health Initiative – Exposure Biology Program Second Annual Grantees Meeting

January 13-15, 2009
Natcher Building, NIH Campus
Bethesda, Maryland

Introduction: The NIH Genes, Environment and Health Initiative's (GEI) Exposure Biology Program (EBP) sponsored a three day meeting of grantees to focus on topics related to the extension of EBP products into practical applications. The meeting began with a day and a half long symposium including sessions focused on validation of sensors and biomarkers; privacy and IRB concerns related to personal monitoring; data analysis; and feedback from epidemiologists on application of products from the EBP to population studies. In addition, the grantees provided updates on research progress in three poster sessions interspersed between these plenary sessions. Individual Steering Committees for each of the program areas met for the final day and a half of the meeting.

The meeting was organized by a planning committee composed of program leads for the four EBP initiatives (*Drs. David Balshaw and Dan Shaughnessy from NIEHS,* Drs. Jill Reedy and Amy Subar from NCI, Dr. Catherine Loria from NHLBI, Dr. Jeffrey Schulden from NIDA, and Dr. Kay Wanke from OBSSR) and principal investigators from each program area (Dr. Joel Pounds from PNNL, Dr. Charles Rodes from RTI, Dr. Carol Boushey from Purdue University, Dr. Vivek Shetty from UCLA and Dr. Santosh Kumar from the University of Memphis). The meeting was attended by 175 registered participants consisting of principal and co-investigators and students from the funded projects as well as program staff and project scientists from NIEHS, NCI, NHLBI, NIBIB, NINDS, NIAID, NIDA, and NIAAA.

Meeting Highlights: The meeting began with a welcome and introduction by *Dr. Gwen Collman* consisting of highlights and accomplishments in the EBP during the last year, including workshops and presentations by Exposure Biology grantees at national scientific meetings. Following the introductory presentation, the first session covered topics on validating biomarkers, dietary and physical activity assessment tools and validation of data collected from personal monitors of chemical exposure. Speakers included Dr. David Cella (Northwestern University), Dr. John Groopman (Johns Hopkins School of Public Health), Dr. Subar, Patty Freedson (University of Massachusetts at Amherst), and Dr. Rodes. These speakers presented their experiences and words of wisdom of issues faced in the validation of products similar to those being developed in the GEI.

Next, a panel of epidemiologists representing topics from each of the four program areas presented brief overviews of population studies they are conducting and discussed promises and challenges of applying tools for measuring personal exposure and response in these studies. Panelists included Dr. Rob McConnell (University of Southern California), Dr. James Lockey (University of Cincinnati), Dr. Linda Van Horne (Northwestern University), Dr. Charles Matthews (Vanderbilt University), and Dr. Arun Karlamangla (University of California, Los Angeles). A major point of discussion for the panelists was the balance between an 'if you build it they will come' reality and a need for a demonstration that the tool to be used can cost-effectively provide superior information to what is already available.

The first day closed with a session on privacy and IRB considerations and covered numerous issues arising from application of personal monitoring tools and featured talks by Dr. Bradford Hesse (NCI) and Dr. Mani Srivastava (University of California, Los Angeles CENS program). These presentations highlighted the use of technological solutions to ensure the protection of sensitive information while simultaneously allowing scientific use of the information by the investigators.

The second day began with a session on data analysis that included talks by Dr. Gary Fogel (Natural Selection, Inc.) on neural network and machine-learning approaches to analyzing complex data, Dr. Greg Farber (National Center for Research Resources) on the resources and opportunities for data sharing afforded through the Biomedical Informatics Research Network, and Dr. Steven Boker (University of Virginia) on the challenges of capturing and storing data from real-time collection streams.

Dr. Balshaw gave concluding remarks, emphasizing the focus of the Experimental Biology Program and stressing that as the projects mature they need to increasingly focus on the final application of their products in population based studies. He also provided updated information on applying for Opportunity Fund supplements for the current year.

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Outstanding New Environmental Scientist Grantee Forum
December 11, 2008
NIEHS, Research Triangle Park, North Carolina

The Outstanding New Environmental Scientist (ONES) Award is a Grant Program to identify outstanding junior scientists in the University-based community who have a long term career commitment to research in the environmental health sciences. The ONES is a research grant that includes funding for an outstanding research project, equipment, and career enhancement activities to enable awardees to launch an innovative research program focusing on problems of environmental exposures and human biology, human pathobiology and human disease.

The ONES Award has been announced as a request for applications once a year for the past three years. Following the award of the grant, recipients are invited to the NIEHS campus to present their research and to become acquainted with the NIEHS campus and research community. In addition to presenting their research at an NIEHS wide research forum, the awardees had lunch with the Division of Extramural Research Program Officers, visited with members of the NIEHS Postdoctoral Association, and visited laboratories and met with Intramural Scientists.

The ONES Awardees for 2008 were:

PI Name	Title	Institution
Pi, Jingbo	Paradoxical roles of Nrf2 activation in arsenic-induced beta-cell dysfunction	The Hamner Institutes
Slitt, Angela	Effect of nutritional status on MRP2 expression and biliary excretion of bisphenol	University of Rhode Island
Stapleton, Heather	Children's exposure to flame retardants: Effects on thyroid hormone regulation	Duke University
Hollingsworth, John	Ozone primes pulmonary innate immunity	Duke University
Bowman, Aaron	Gene-environment interactions between manganese exposure and Huntington disease	Vanderbilt University
O'Neill, Marie Sylvia	Air pollution, inflammation and preterm birth: A mechanistic study in Mexico City	University of Michigan. Ann Arbor

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NIEHS Superfund Research and Training Program 2008 Annual Meeting:
Innovative Science and Technology for Mitigating Human, Ecological, and Environmental Risks
December 7-9, 2008
Asilomar Conference Center
Pacific Grove, California

Introduction: Over 200 Superfund grantees, researchers, partners, post-doctoral fellows and graduate students gathered for the 11th NIEHS Superfund Research and Training Program annual meeting, held December 7-9, 2008 at the Asilomar Conference Center in Pacific Grove, California.

Highlights: Two keynote speakers were featured at the meeting. On Monday, Dr. Arlene Blum, visiting scholar at the University of California, Berkley, and author of *Annapurna: A Woman's Place* and B*reaking Trail: A Climbing Life,*" described the environmental impacts of fire retardants used in the home in her presentation, entitled "The Fire Retardant Dilemma: Balancing Safety, Human Health, and Environmental Protection." On Tuesday, Dr. Martin Kenney, Professor of Human and Community Development at the University of California, Davis, advocated for individual ownership of the patents and products of intellectual property developed within university systems in his presentation, "Is the Mandatory Invention Ownership University Technology Licensing Office the Best Method of University Technology Transfer?"

Four plenary sessions highlighted student and researcher/post-doc advances in environmental health. Sessions focused on analytical/bioanalytical advances; fate, transport and remediation; and methodologies, toxic effects of superfund chemicals, and exposure, risk, and epidemiology. In addition, a panel discussion was held to discuss real-world applications of Superfund technologies and methodologies

As has come to be a tradition, the winner of the 2008 Karen Wetterhahn Memorial Award was made. This year the recipient of the award was Ms. Laura Senier. Following the award presentation, she delivered a talk on her research, "Public Schools and Contaminated Land in Rhode Island: Using SBRP Research Translation and Community Outreach to Foster Research and Advocacy", to an audience of 200.

Student poster sessions were held on Sunday and Monday evenings. One student from each session was honored for their presentation efforts. Stephen Richardson (University of North Carolina, Chapel Hill) and Courtney Kozul (Dartmouth University) each received a cash prize and an autographed copy of Arlene Blum's book, *Breaking Trail: A Climbing Life*.

*****

Fourth Annual Early Environmental Exposures Meeting
November 13-14, 2008
Birmingham, Alabama

Background: The Breast Cancer and the Environment Research Centers (BCERC) Network originated in September 2003 in response to a congressional mandate with support from both the breast cancer advocacy and research communities. This seven-year program aims to advance the understanding of environmental factors that influence mammary gland architecture and the entry and progression through female puberty. The studies are conducted by four collaborating centers at Fox Chase Cancer Center (Dr. Jose Russo); University of California, San Francisco Dr. Robert Hiatt), University of Cincinnati (Robert Bornschein), and Michigan State University (Dr. Sandra Haslam).

Objectives: The BCERC Network is pursuing epidemiological and biological studies investigating the influence of Early Environmental Exposures on pubertal maturation, mammary gland development, and the potential of these exposures to alter the risk of breast cancer later in life. The latest scientific findings from the BCERC were presented along with results from investigations in other studies in the field. The content of the meeting included basic biology of breast development, environmental exposures that

influence puberty, breast development and future breast cancer risks, and public health communication of the risks associated with these exposures.

Highlights and Recommendations: This year's annual scientific meeting focused on the integration of laboratory-based biology and epidemiology studies in research programs while continuing to assimilate community participation and advocacy concerns through panel discussions, a Mentoring Session, and "Lunch with the Experts", an opportunity for attendees to share their thoughts over lunch with speakers and investigators.

Dr. Gwen Collman, Interim Director, DERT, made opening remarks to the assembled group. *Dr. Les Reinlib, SPHB*, represented NIEHS in the final Panel Discussion with the Audience. *Dr. Elizabeth Maull, SPHB*, helped organize and attended the meeting. Research updates from the members of the BCERC Network, as well as platform presentations from invited speakers, including a keynote address by Dr. Andreas Kortenkamp, University of London, provided thoughtful perspectives to the participants on studies related to mammary gland biology, puberty, and breast cancer as well as the action of environmental chemicals and diet on the developing breast.

The NIEHS, NCI, and Avon Foundation were able to provide partial travel support for a number of advocates and young scholars. The symposium was videotaped and will be made available to the public through the BCERC web-site (http://www.bcerc.org/home.htm) in the near future. Drs. Reinlib and Maull, oversaw the organization of the meeting and contributed to planning the scientific sessions.

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The Central and Eastern European Conference on Health and the Environment: the Environment - A Platform for Health
October 19-22, 2008
Cluj-Napoca, Romania

Background: Based on the concept that the research of the last decades has demonstrated that many diseases are related to the poor quality of the environment, an international conference was convened to analyze and better define the complex links between health and environment. Over 250 participants, mostly from central and eastern Europe, discussed the specific problems of their regions; but presentations incorporated issues related to other parts of the world as the major meeting themes were universal in nature.

This was the third in a series of Central and Eastern European conferences which built on the successes of its predecessors in Prague 2004 and Bratislava 2006.

Highlights: The conference was formatted to encourage collaboration among scientists from various fields, increase interdisciplinarity and multinational participation, and promote integrative research. The major environmental issues of the regions were addressed during the science sessions: sustainable mining, risk assessment and management, environmental health and children's health.

The conference was preceded by workshops on responsible mining, conducting international collaborative research, use of biomarkers, and childhood exposures.

A highlight of the meeting was the strong focus on student participation. There were four breakouts devoted to student presentations, representation of students' research during the poster sessions and a special student discussion session where an international panel of eight students responded to hot topic environment issues. It is anticipated that this discussion will result in a student initiated publication.

Dr. Claudia Thompson, Acting Director of CRIS, presented a keynote, New Tricks for an Old Poison: Use of "-omics" to Study Arsenic Effects. *Ms. Beth Anderson, CRIS*, served on the program committee, was a

session chair and presented summary remarks regarding the students sessions during the closing session.

*****

International Environmental Nanotechnology Conference: Applications and Implications
October 7-9, 2008
Hyatt Regency Hotel
Chicago, Illinois

Background: Nanomaterials present new opportunities to improve our ability to detect, monitor, control and remediate pollutants; however, potential new risks to human health and the environment are a concern that deserves attention. Hence, the U.S. EPA has endeavored to bring together researchers to address the overarching theme of "environmental nanotechnology" beginning with a conference in Washington, DC (October 2005), and another in Chicago, Illinois (September 2006). This past October represented a continuation of these meetings, led by Region 5 EPA and partners at the NIEHS/SBRP, the Agency for Toxic Substance and Disease Registry (ATSDR), the National Science Foundation (NSF), the Department of Energy (DOE), the U.S. Army, the U.S. Navy, and the University of Chicago's Great Lakes Centers for Occupational and Environmental Safety and Health.

Meeting Highlights: EPA Region 5 Deputy Regional Administrator, Mr. Bharat Mathur, opened the conference by welcoming the participants and remarking on the importance of nanotechnology to Region 5 and EPA in general. Mr. Mathur was followed by former EPA Assistant Administrator for Research and Development, Dr. George Gray, who provided perspective on nanotechnology and activity of the Office of Research and Development. EPA National Program Director for Nanotechnology, Mr. Jeff Morris, followed Dr. Gray with commentary on U.S. Federal Interagency activities and international environmental nanotechnology collaborations.

The conference brought together researchers and practitioners from around the world to discuss the nanotechnology applications for remediation of environmental contaminants; the implications of releasing manufactured nanoparticles into the environment; and opportunities for monitoring and sensing. The international character of the meeting was highlighted by nanotechnology experts from Australia, France, Ireland, Japan, Korea, the Netherlands, the United Kingdom, and the United States who provided keynote commentaries on the focus areas of the conference program: remediation, nano-enabled sensing, fate and transport, biological exposure, and toxicity. In addition, lunchtime plenary addresses were given by Dr. Martin Philbert (University of Michigan) and Dr. Igor Linkov (U.S. Army Core of Engineers). The conference agenda included over 100 presentations and 40 posters for the approximately 185 attendees.

Outcomes/Recommendations: Researchers reinforced the benefits of international collaborations in addressing the tremendous potential of nanotechnology. Concerted efforts to standardize minimal information needed in toxicology studies show early indications that there is cross-talk between nations. Furthermore, the development of safe and exciting technologies to make remediation/monitoring efforts more effective will be universally beneficial.

Superfund Basic Research Program staff *Drs. Claudia Thompson and Heather Henry and Ms. Beth Anderson* attended the meeting.

*****

Environmental Health Sciences (EHS) Core Center Annual Meeting
October 19-21, 2008
Philadelphia, Pennsylvania

Background: *Dr. Les Reinlib and Mr. Liam O'Fallon, SPHB,* worked with University of Pennsylvania Center staff to organize the 2008 EHS Core Center meeting with a key scientific theme on "Omics"

Approaches in Environmental Health Sciences. The meeting was comprised of concurrent and joint sessions of science and outreach staff.

Highlights: *Dr. William Suk* delivered the NIEHS Update to all meeting participants, highlighting scientific and administrative accomplishments over the past year and plans for the future. At the Community Outreach and Education Core (COEC) session, *Dr. Christie Drew, PAB*, gave a well-received presentation on evaluation and logic models. Mr. O'Fallon presented on the Partnerships for Environmental Public Health (PEPH) program.

During the joint session designed to prompt recommendations from Center Directors and COEC staff, Dr. Reinlib presented on the NIEHS Exposure-Biology Program. After Dr. Reinlib's presentation, he and Mr. O'Fallon fielded questions and facilitated discussion on topics of interest. The issue of greatest interest was the development of standard operating procedures for sharing biospecimens.

Recommendations: It was recommended that a working group of Center Directors be created to consider in greater detail the issue of sharing biospecimens.

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Pacific Southwest Residuals Symposium
October 1-2 2008
University of California, Davis; Davis, California

Background: The Third Annual Pacific Southwest Organic Residuals Symposium brought together industry professionals, municipalities, regulators and other stakeholders to identify and realize opportunities that provide the greatest ecological and municipal benefits for using manures, biosolids and other organic residuals. Sponsors were the U.S. EPA (Pacific Southwest Region 9), NIEHS' Superfund Basic Research Program (SBRP), California Integrated Waste Management Board, California State Water Resources Control Board, California Department of Food and Agriculture, Sustainable Conservation, California Association of Sanitation Agencies, Western United Dairymen, and the Association of Compost Producers.

Highlights: The theme of the meeting was Recycling Organic Residuals: Achieving Net Environmental Benefits. In relation to the support by the SBRP under NIEHS, there were two sessions on antimicrobials: (1) Antimicrobial Compounds in Consumer Products and Biosolids: Environmental Occurrence, Fate, and Exposure chaired by: Dr. Rolf Halden, Arizona State University and (2) Antimicrobials: Human Exposure and Health Effects chaired by Dr. Dan Chang, Professor Emeritus, UC Davis. Two antimicrobials, triclosan (TCS) and triclocarban (TCC) that are high volume and in many consumer products (hand soaps, tooth paste, etc), were discussed in terms of their presence in biosolids, persistence in the environment as well as new findings with respect to *in vitro* nerve and *in vitro/in vivo* hormonal activities and data on human exposure.

TCC and TCS bear structural and physico-chemical similarities to Superfund chemicals and were recently tested in biomarker assays developed by the SBRP. Evidence of potential endocrine disruption (ED), effects on enzymatic pathways, as well as neurotoxicity have been observed in mechanistically-derived human cell-based receptor assays, and limited confirmation of endocrine disruption has been presented for TCC in an animal model. Measurements of significant exposure in the U.S. population (75%) to TCS were recently reported by the CDC NHANES program (Calafat Environ Health Perspect, 2008, 116(3): 303–307). Limited tests of exposure to TCC in volunteers indicate exposures can lead to blood levels close to those which resulted in significant effects in the receptor-based assays. Limited data on changes in soil bacterial populations, ED in aquatic species and entry in the food chain have also recently being reported.

These scientific findings were conveyed to manufacturers, affected industries (wastewater treatment) and regulators. Interested parties from diverse fields of research presented and discussed the potential implications of their recent findings.

In attendance from NIEHS/SBRP were Dr. Claudia Thompson, Acting Director SBRP and Ms. Beth Anderson, CRIS Program Analyst.

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Global Variability in Response to Air Pollution: Approaches to Translation of Cardiopulmonary Disease Models
September 4-5, 2008
Chapel Hill, North Carolina

Background: This conference was held as a recommended follow-up to a small workshop held in conjunction with the 2007 International Society of Environmental Epidemiology meeting in Mexico City that explored air pollution studies around the globe. A specific recommendation from the 2007 workshop was to hold a larger conference to bring the animal modelers together with human geneticists and epidemiologists to further advance this field. This conference was intended to foster collaborations between human disease and mouse model researchers so they can expedite identification of genetic susceptibility loci and gene-environment interactions relevant to human diseases associated with air-pollution exposure. This conference also aimed to identify appropriate strategies and approaches for combining and complementing research efforts in human population and animal studies to advance an understanding of the biological pathways involved in air pollution-induced human diseases. The conference began with three overview presentations that presented the state of the science on air pollution and cardiovascular health, pulmonary disease, and genetic susceptibility research. The majority of the remaining conference time focused on three scientific sessions (Genetic Susceptibility of Cardiopulmonary Diseases, Mechanisms of Action/Translation, and Genetics to G x E Interactions and Methods). A final implementation session identified the most important concepts and recommendations.

Numerous themes related to translation of this research field emerged from this conference. The complexity of studying the effects of air pollution was emphasized with the recognition that multiple mechanisms probably account for the impact of air pollution on cardiopulmonary outcomes including: vasoconstriction, clotting/endothelial dysfunction, autonomic nervous system, and inflammation. Many investigators commented on the necessity of bidirectional and interdisciplinary work to allow studies flowing from animal to human and human to animal to validate prior findings and the need for better integration of human-animal data. Multiple issues related to the acute versus chronic effects of air pollution response were discussed with the recognition that the biological pathways involved in acute versus chronic outcomes may be different. Many participants commented on the challenge of extrapolating acute effects seen in challenge or panel studies with the mostly chronic effects studied in epidemiological investigations and the need for biomarkers of chronic effects. The importance of replication of findings, particularly with respect to G x E interaction studies, was stressed. The requirement for more robust analytical and computational tools was recognized for dealing with huge datasets and G x E studies. The many useful mouse resources available today to study G x E and biomarkers of response were described extensively, including: recombinant inbred strains; systems genetics approaches in mice; and the Collaborative Cross, a collection or resource of mouse strains to be used as a tool in mouse genetics.

Recommendations: Specific recommendations to move forward were made throughout the conference and were reiterated at the final implementation session. Many investigators felt that replication studies could be facilitated and streamlined by the establishment of “replication networks” among several institutions. Replication networks should be systematized, standardized, multi-site networks for thoughtful replication of human and laboratory studies, allowing easy access to collaborators for replication. The establishment of centralized infrastructural resources, such as biobanks, genotyping facilities, and computational resources was also stressed. More resources were called for to pool analyses from similar

animal model experiments and to facilitate meta-analysis on pooled analysis of human outcomes data. Many scientists recommended that NIEHS put more emphasis on training needs as well. Specific training suggestions included: the use of multiple mechanisms of individual and institutional training, allowing the training of foreign postdoctoral fellows, and the need for computational/toxicology training and other trans-disciplinary training for fellows. Finally, a workshop designed to discuss approaches for standardization of common exposure measures (including what particles, what timing, and dose range) would greatly facilitate collaboration and integration among both American and European institutions and studies.

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Partnerships for Environmental Public Health (PEPH) Workshop
June 30-July 1, 2008
Research Triangle Park, North Carolina

Background: Members of the DERT PEPH Working Group organized the June workshop to engage a diverse set of communities with different perspectives and areas of expertise pertinent to environmental public health. The committee identified certain groups from the responses to the Request For Information (RFI). The organizing committee invited individuals who had familiarity with NIEHS and its mission as well as individuals with little to no familiarity, but who were leaders in a field that could benefit the new PEPH program. The idea was to stimulate new ways of thinking and consider novel approaches to long-standing issues and questions. The organizing committee provided all participants with the RFI Executive Summary and a proposed model for PEPH so that they could ground their feedback and comments on the report and model.

The organizing committee structured the workshop around three key sessions that focused on a specific question (see below). Each session had three components: an introductory panel, break-out discussions and a report-back period. The introductory panel was comprised of five to seven participants each sharing their views. After any clarifying questions, attendees split into four pre-assigned break-out groups. The break-out groups engaged in a discussion related to the designated question for that session. At the end of the break-out discussion, all workshop attendees reconvened to share the most significant concepts discussed in the break-out groups.

Session Questions

1) In the environmental public health field, what issues and un-met needs are faced in the areas of building capacity, evaluation, communication, and research?
   What are the most important Tools needed?
   What creative new Strategies can be used?
   What Resources are needed (beyond money)?
   What Partnerships should be fostered?

2) What is NIEHS' unique role in helping identify and foster solutions to the following:
   Building capacity
   Evaluation
   Communication
   Research

   How would you balance and prioritize the diversity of critical areas/needs in EPH?

Key Recommendations: Workshop participants shared many valuable recommendations to NIEHS staff members. The recommendations were organized into the following categories: Criteria and Concepts for PEPH, Products, and Processes and Activities. Participants emphasized the need for PEPH to be nimble, support gold standards, advance research to action, and, as an umbrella program, it must promote integration across the five proposed areas of PEPH. Recommendations regarding research addressed

four key areas: research topics, evaluation of research, communication of research findings, and research capacity building. Capacity building recommendations focused primarily on the needs of community organizations, community residents, and researchers. With regard to Communication, participants recommended that NIEHS establish itself as a top source for science-based materials on environmental public health, develop communication strategies, enhance science literacy, train effective communicators of environmental health science concepts, work with journals and the media field, and promote information sharing and mentoring. Participant recommendations on evaluation addressed the importance of evaluation within all funded projects, as well as the overall PEPH program. Participants identified key challenges, metrics, and resources. Participants recommended that the PEPH program and the NIEHS develop a variety of different products for the purposes of increasing public awareness of EPH and the institute. Such products included factsheets, webinars, curricular materials, standards, evaluation tools, IRB guidelines, and cumulative exposure tools and methods. Participants also enumerated a variety of processes and activities that the NIEHS and the PEPH program could undertake as the Institute begins to re-establish itself in the field of EPH. Recommendations included activities such as social networking, sustained communication with partners, develop a clear PEPH message, define EPH priorities, market PEPH, evaluate past activities, and develop metrics for future activities.

The full Workshop Summary will be posted to the PEPH website in February:
http://www.niehs.nih.gov/research/supported/programs/peph/index.cfm

Questions should be directed to Mr. Liam O'Fallon at ofallon@niehs.nih.gov.

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DERT PAPERS OF NOTE

Selenium May Prevent High-Risk Bladder Cancer
Margaret R. Karagas, Ph.D.
Dartmouth Medical School
P42ES007373

NIEHS-supported grantees at Dartmouth Medical School report in a new study that selenium may help prevent high-risk bladder cancer. The study found that women, moderate smokers, and people p53 positive tumors showed significant reductions in bladder cancer with higher selenium intake.

In the US, bladder cancer is the fourth most common cancer among men and twelfth most common among women with approximately 67,000 cases being diagnosed each year. About 13,000 deaths are expected this year from bladder cancer. Bladder cancer develops through different pathways, but one of the major paths is through alterations in the p53 gene. These cancers are associated with more advanced disease.

The study involved 857 people with newly diagnosed bladder cancer. Selenium intake was measured by analyzing toenail clippings. Cancer risk was reduced between 30 and 50 percent in the three groups as selenium intake increased.

The exact mechanism by which selenium inhibits carcinogenesis is unknown, but it may occur through several mechanisms including reducing oxidative stress and inflammation, enhanced immune responses, activation of DNA repair genes, etc. The results of this study may provide clues on how to prevent tumors from developing and potentially lead to new chemotherapeutic agents.

Citation: Wallace K, Kelsey KT, Schned A, Morris JS, Andrew AS, Karagas MR. Selenium and risk of bladder cancer: a population-based case-control study. Cancer Prev Res (Phila Pa). 2009 Jan;2(1):70-3.

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Gene Packaging is Important in Cancer
Stephen B. Baylin, MD
The Johns Hopkins University Medical Institutions
R01ES011858

New NIEHS-supported research from Johns Hopkins University suggests that the packaging of genes may be as important as the genes themselves when it comes to the development and treatment of cancer. The findings point to the three dimensional chromatin packaging around genes formed by tight loops of polycomb group proteins. Chromatin packaging is a complex combination of DNA and proteins that compress the DNA to fit inside the cell nucleus. The effect of the tight packing and polycomb proteins is to keep genes in a low expression state.

The researchers compared embryonic cells to adult colon cancer cells. The gene studied, GATA-4, is packaged by polycomb group proteins. In the embryonic cells the gene is in a low expression state and had no methylation. When the gene received signals for the cells to mature, the protein structures were disrupted and the gene was highly expressed. However, when the same gene was methylated, as is the case in the colon cancer cells, the polycomb protein packaging loops were tighter and there was no gene expression. When the researchers removed the methylation, the cancer cells behaved similarly to the embryonic cells.

DNA methylation is a normal cellular process, but when the normal processes are disrupted and some genes are improperly methylated, it can shut down important tumor suppressing cell functions. Drugs that removed abnormal DNA methylation from genes have been introduced as potential cancer therapies. This research suggests that for these therapies to be fully effective, researchers may need to search for agents that disrupt the polycomb protein loops.

Citation: Tiwari VK, McGarvey KM, Licchesi JD, Ohm JE, Herman JG, Schübeler D, Baylin SB. PcG proteins, DNA methylation, and gene repression by chromatin looping. PLoS Biol. 2008 Dec 2;6(12):2911-27.

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Dopamine Transmission Impaired by Manganese
Tomás R. Guilarte, Ph.D., Neal C. Burton, Johns Hopkins Bloomberg School of Public Health
NIEHS Grants R01ES010975 and T32ES007141

NIEHS grantees at Johns Hopkins University report that manganese exposure inhibits dopamine neurotransmission from the *substantia nigra* region of the brain leading to motor activity impairments. These results follow on previous studies from this laboratory using cynomologus macaques, also known as crab-eating macaques or long-tailed macaques. Previous research has shown that these monkeys have slight cognitive and fine motor deficits in response to manganese exposure.

The debilitating neurological condition manganism results from chronic high-dose exposure to the essential trace mineral manganese. Movement abnormalities associated with manganism resemble the same condition in Parkinson's disease. Manganese-induced parkinsonism most often results from high exposure in industrial settings related to steel production; however other sources include the impairment of manganese excretion in some liver diseases, patients receiving high doses of manganese from parenteral nutrition, the injection of illicit psychostimulant drugs containing manganese, and possibly exposure to ambient concentrations of manganese generated from gasoline containing the additive methylcyclopentadienyl manganese tricarbonyl.

The monkeys were treated weekly with manganese doses ranging from 3.3-10 milligrams per kilogram body weight from seven up to 59 weeks. They received PET scans prior to the beginning of dosing and at one or two times points during the exposure. The researchers found that amphetamine-induced dopamine release was markedly reduced in the manganese-exposed animals. They conclude that the manganese

exposure is responsible for the motor deficits documented in the monkeys. These findings may have implications for the prevention and treatment of symptoms of parkinsonism.

Citation: Guilarte TR, Burton NC, McGlothan JL, Verina T, Zhou Y, Alexander M, Pham L, Griswold M, Wong DF, Syversen T, Schneider JS. Impairment of nigrostriatal dopamine neurotransmission by manganese is mediated by pre-synaptic mechanism(s): implications to manganese-induced parkinsonism. J Neurochem. 2008 Dec;107(5):1236-47.

Note: Neal Burton is a PhD student and was honored at the Society of Toxicology's Annual Meeting in March 2006. Burton brought home first prize in the Neurotoxicology Specialty Section competition for his poster titled "In Vivo Attenuation of the Parkinsonian Phenotype by Induction of the Keap1-Nrf2 Pathway."

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Dioxin Disrupts Prostate Development
Thomas A. Gasiewicz, Ph.D., University of Rochester Medical Center and
Chad M. Vezina, Ph.D, and Richard E. Peterson, Ph.D., University of Wisconsin Madison
R01ES009430, P30001247 (TAG), F32ES014284 (CMV), and R37ES001332 (REP)

Researchers at the University of Wisconsin in Madison have determined the mechanism by which dioxin disrupts prostate gland formation in laboratory mice. They found that when dioxin is administered maternally at between days 15 and 16 of gestation, the chemical inhibits the formation of certain prostate buds in two different regions (ventral and dorsolateral).

Members of this research team have previously shown that dioxin exposure during the fetal and neonatal periods decreases prostate size in mice and later that fetal dioxin exposure inhibited prostate budding thereby reducing the number of prostate ducts and causing the reduction in prostate size. There is also a growing body of scientific evidence that dioxin exposure in humans causes prostate cancer.

Experimental results show that hyperactivation of the aryl hydrocarbon receptor signaling pathway changes the patterning of the fetal urogenital sinus, and disrupting where prostate buds develop and where prostate lobes are formed. The current study presents a new paradigm of how *in utero* dioxin exposure disrupts prostate formation suggesting this same mechanism may in part explain how dioxin impairs the development of other organs and tissues.

Citation: Vezina CM, Allgeier SH, Moore RW, Lin TM, Bemis JC, Hardin HA, Gasiewicz TA, Peterson RE. Dioxin causes ventral prostate agenesis by disrupting dorsoventral patterning in developing mouse prostate. Toxicol Sci. 2008 Dec;106(2):488-96.

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Microglial Cell Enzyme Involved in Neuronal Cell Death
Michael Karin, Ph.D.
University of California at San Diego
R01ES006376

An international research team at the University of California San Diego and the Seoul National University funded by NIEHS report the discovery of the involvement of micoglial cell IκB kinase in excitotoxin-induced neurodegeration. This discovery identifies a target for preventing mass cell death following traumatic brain injury, stroke, or as a result of neurodegenerative diseases.

Excitotoxicity is the process by which nerve cells are damaged and killed by excitotoxins such as glutamate, N-methyl-D-aspartic acid (NMDA), kainic acid, and others. This occurs when neurotransmitter receptors are overstimulated by these and other excitotoxins allowing high levels of calcium ions to enter the nerve cells. The influx of calcium goes on to activate a number of enzymes that lead to damaged cell structures such as the cytoskeleton, the cell membrane, and DNA.

The team employed a special strain of knock out mice that have no gene for the IκB kinase enzyme in specific cells of myeloid lineage including microglia, cells that act as the first and main form of active immune defense in the central nervous system. The gene deletion reduced the IκB kinase activity in cultured microglia by up to 40 percent compared to microglia from normal mice. Kainic acid-induced hippocampal neuronal cell death was reduced by 30 percent in the knock-out microglia. The reduction in neuronal cell death was followed by decreases in kainic acie-induced glial cell activation and expression of proinflammatory genes such as tumor necrosis factor, and interleukin. Additional studies utilizing brain tissue slices in culture showed decreased susceptibility to kainic acid-induced excitotoxicity in knock-out mice brain tissue.

As a result of these studies, the researchers conclude that IκB kinase dependent microglia activation plays a role in kainic acid-induced neuronal cell death by induction of inflammatory agents. The discovery identifies IκB kinase as a possible target for therapeutic interventions to ameliorate or prevent additional cell death following serious brain injuries or as a result of neurodegenerative disease.

Citation: Cho IH, Hong J, Suh EC, Kim JH, Lee H, Lee JE, Lee S, Kim CH, Kim DW, Jo EK, Lee KE, Karin M, Lee SJ. Role of microglial IKKbeta in kainic acid-induced hippocampal neuronal cell death. Brain. 2008 Nov;131(Pt 11):3019-33.

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Discovery of Gene Variant for Cleft Lip

Jeffrey C. Murray, MD, Department of Pediatrics, University of Iowa and
Allen J. Wilcox, MD, Ph.D., NIEHS
P30ES005605

About one-fifth of isolated cleft lip may be due to a single nucleotide difference in the DNA sequence of a gene involved in facial development, according to new research findings from an international research team funded in-part by NIEHS and including an NIEHS intramural scientist. Isolated cleft lip, meaning the child has no other abnormalities, is one of the most common birth defects. The researchers say this discovery could lead to DNA tests to help couples better understand their risk of having a child with a cleft lip.

During fetal development, the lip normally fuses around 35 days of gestation. Since failure of lip fusion can impair the subsequent closure of the palatal shelves, cleft lip is often accompanied with cleft palate. If normally developed parents have a child with an isolated cleft lip, the risk of their second child having a similar cleft increases. Along with other recent gene discoveries, the research team reports they can now account for approximately 30 percent of isolated cleft lip. Just 25 years ago, there had yet to be a single gene identified.

This research finding began six years ago when the team discovered that a gene called IRF-6 is involved with a rare condition called Van der Woude syndrome. About 15 percent of people with the syndrome have malformations that are clinically indistinguishable from isolated cleft lip, which suggested that the gene might be involved in both conditions. Through studying the gene's sequence they discovered a single sequence variant in a section of DNA that is almost identical across twelve different animals.

The team determined that the substitution of a single adenine molecule in place of a guanine in the IRF-6 gene alters the binding site for a protein called AP-2a. The protein is known to be involved in craniofacial development and when altered, causes a syndrome that involves clefts. These findings may not only lead to improvements in predicting clefts, but possibly better interventions to prevent them.

Citation: Rahimov F, Marazita ML, Visel A, Cooper ME, Hitchler MJ, Rubini M, Domann FE, Govil M, Christensen K, Bille C, Melbye M, Jugessur A, Lie RT, Wilcox AJ, Fitzpatrick DR, Green ED, Mossey PA,

Little J, Steegers-Theunissen RP, Pennacchio LA, Schutte BC, Murray JC. Disruption of an AP-2alpha binding site in an IRF6 enhancer is associated with cleft lip. Nat Genet. 2008 Nov;40(11):1341-7.

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Antioxidant Administration Reduces Lung Injury from Chlorine Exposure

Edward Postlethwait, Ph.D. and Sadis Matalon, Ph.D.
University of Alabama at Birmingham
U01ES015676

Dosages of vitamin C and other low molecular weight antioxidants may help prevent chlorine-induced lung injury that occurs after railroad tanker spills or might occur as a result of terrorist attacks according to NIEHS-supported research from the University of Alabama Birmingham. The levels of chlorine exposure used in the research study mimic those seen during accidental exposures.

Chlorine is a powerful oxidant that is used in bleaches, disinfectants, and in a wide variety of industrial processes. Under normal conditions, it is a pale green gas that is denser than air. Thousands of tons of chlorine gas are transported by rail in the US each year. Recently chlorine rail cars have been suggested as targets for terrorist attacks. Media reports suggest that as many as 100,000 people could be killed or seriously harmed from the explosion of a single railroad tank car traveling through a major city.

The research team exposed laboratory rats to chlorine gas at either 184 or 400 parts per million for 30 minutes in controlled environmental chambers. These levels are similar to those measured near chlorine tanker spills. Just one hour after exposure, the rats showed evidence of decrease arterial blood oxygen, increased blood carbon dioxide and acidosis, and increased markers of inflammation in respiratory fluid samples. In a subsequent experiment, administration of a mixture of antioxidants, which included ascorbic acid (vitamin C), deferoxamine, and N-acetyl-L-cysteine, prior to exposure to 184 parts per million of chlorine dramatically reduced the respiratory effects seen in the previous experiment.

These experiments suggest that antioxidant administration may be useful for preventing the serious lung injury and death that can occur as a result of chlorine gas exposure. Additional studies will be necessary to confirm these findings, but these results suggest that hazardous materials responders and rescue crews may benefit from prophylactic antioxidant administration prior to responding to a chlorine spill.

Citation: Postlethwait E, Matalon S. Mitigation of chlorine-induced lung injury by low-molecular-weight antioxidants. Am J Physiol Lung Cell Mol Physiol. 2008 Nov;295(5):L733-43.

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Consumption of Foods with High Soy Content is Associated with Lower Sperm Concentrations in Men

Russ Hauser, MD, Ph.D.
Harvard School of Public Health
R01ES009718 and P30ES000002

New research from the Harvard School of Public Health reports that men who eat a high amount of soy-based food products have lower total sperm counts. Soy is rich in estrogenic compounds known as isoflavones including genistein, daidzein, and glyciten.

The medical literature is replete with reports of steep drops in sperm count over the last 60 years in the U.S. and Europe. Possible explanations implicate increased exposure to endocrine disruptors and natural and synthetic estrogens.

In the current study, the 99 research subjects were the male partners of couples being evaluated at the Massachusetts General Hospital Fertility Center. They were asked to complete a questionnaire on the foods they eat regularly which included 15 common soy-based foods including tofu, soy milk, tempeh, tofu

burgers, miso soup, drinks containing soy protein, etc. Men who were in the highest category of soy intake ate one half of a serving each day of a soy-based food. Their sperm counts were on average 41 million sperm per milliliter of semen lower than men who ate no soy foods. Normal sperm counts range from 80 to 120 million per milliliter.

This study suggests that soy foods could have a deleterious effect on sperm production and might need to be avoided by men who have low sperm counts if they are trying to conceive children. The study findings may also be another explanation for why sperm counts are dropping worldwide.

Citation: Chavarro JE, Toth TL, Sadio SM, Hauser R. Soy food and isoflavone intake in relation to semen quality parameters among men from an infertility clinic. Hum Reprod. 2008 Nov;23(11):2584-90.

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Parkinson's Disease Linked to Vitamin D Deficiency

Mahlon R. DeLong, MD
Emory University School of Medicine
U54ES012068

Fifty–five percent of Parkinson's disease (PD) patients are insufficient in vitamin D, according to new research findings from an NIEHS-supported study at the Emory University School of Medicine. The number of Parkinson's patients with vitamin D deficiency was higher than either healthy elderly people in the control group or Alzheimer's disease patients. This finding adds to the evidence that low vitamin D levels are associated with Parkinson's disease.

Most Americans get sufficient amounts of vitamin D through exposure to sunlight or by dietary supplements. Vitamin D fortified milk or cereals are a minor source of the vitamin and few foods, such as fatty fish like salmon or tuna, contain substantial amounts of vitamin D. However, the body's ability to produce vitamin D in response to sun exposure decreases with age making elderly people more at risk for vitamin D deficiency.

Currently it is unclear whether there is a cause and effect relationship between vitamin D and Parkinson's. The connection could be partly related to the decreased mobility of Parkinson's patients, which may result in less sun exposure, or that there is a direct link between vitamin D insufficiency and the onset or progression of the disease.

Previous studies have shown that the region of the brain, the subtantia nigra, that produces dopamine and that is most affected by Parkinson's disease, has high levels of vitamin D receptors, suggesting that vitamin D may be important for the normal function of these cells. Emory doctors are conducting additional research to investigate whether vitamin D insufficiency is a cause or a result of having Parkinson's. A follow-up study is administering standard or larger doses of vitamin D to Parkinson's patients to determine if the vitamin supplementation will reduce the severity of their condition.

Citation: Evatt ML, Delong MR, Khazai N, Rosen A, Triche S, Tangpricha V. Prevalence of vitamin D insufficiency in patients with Parkinson disease and Alzheimer disease. Arch Neurol. 2008 Oct;65(10):1348-52.

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Nanoparticles Kill Blood Vessel Cells in the Human Brain
Bernhard Hennig, Ph.D.
University of Kentucky
P42ES007380

A study funded in part by the Superfund Basic Research Program at NIEHS shows that nanoparticles of aluminum oxide can adversely affect and even kill specialized endothelial cells that line blood vessels in the human brain.

The researchers designed this study to determine the effects of nano-scale particles of aluminum oxide on the human blood-brain barrier. In cell culture systems, endothelial cells that line the interior of blood vessels in the brain were treated with nano-alumina, normal sized alumina particles, carbon nanoparticles, or normal sized carbon particles. After exposure, the researchers assessed cell structure, cell death, mitochondrial effects, and tight junction proteins. Laboratory rats were given intravenous doses of nano-alumina.

In 2005, aluminum oxide nanoparticles accounted for 20 percent of the world production of nanoparticles. The particles are used in a variety of applications in the ceramics, electrical, engineering, and biomedical fields. Increases in the production and expansion of the uses of these particles will inevitably lead to greater human exposure.

The nanoscale alumina and carbon particles were much more toxic than their respective compounds of normal particle size. Nano-alumina significantly increase cellular oxidative stress and disrupted the expression of tight junction proteins. The whole animal experiments confirmed the protein alteration with a loss of critical proteins in the cerebral blood vessels.

Citation: Chen L, Yokel RA, Hennig B, Toborek M. Manufactured aluminum oxide nanoparticles decrease expression of tight junction proteins in brain vasculature. J Neuroimmune Pharmacol. 2008 Dec;3(4):286-95.

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Cytosine-DNA Methyltransferase Mediates Carcinogen-Induced Gene Promoter Methylation
Steven A. Belinsky, Ph.D.
Lovelace Respiratory Research Institute
R01ES008801

NIEHS-supported researchers studying the basic cellular and molecular events that occur after exposure to carcinogens report differences in DNA repair capacity in bronchial epithelial cell lines after low-dose treatment with methyl-nitrosourea and benzo(a)pyrene-diolepoxide. They also found that levels of cytosine-DNA methyltransferase 1 (DNMT1) increased significantly during the carcinogen exposure and were linked to promoter-hypermethylation of several genes in each transformed cell line. These finding may have implications for preventing lung cancer in smokers.

When the researchers employed strategies to reduce the production of the DNMT1 protein, cell transformation and gene silencing were reversed. Reduced DNMT1 production prior to carcinogen exposure prevented transformation and gene methylation.

These studies and findings describe a mechanistic link between increased DNMT1, methylation of tumor suppressor genes and reduced DNA repair capacity that together appear to cause cancer-like changes in lung epithelial cells. The study also provides evidence for the use of demethylation strategies to prevent lung cancer in smokers.

Citation: Damiani LA, Yingling CM, Leng S, Romo PE, Nakamura J, Belinsky SA. Carcinogen-induced gene promoter hypermethylation is mediated by DNMT1 and causal for transformation of immortalized bronchial epithelial cells. Cancer Res. 2008 Nov 1;68(21):9005-14.

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Gas Stove Emissions Worsen Asthma Symptoms

Patrick N. Breysse, Ph.D., MHS, and Gregory B. Diette, MD, MHS
Johns Hopkins University
P01ES009606

Johns Hopkins scientists supported by NIEHS report that high levels of nitrogen dioxide gas from cooking and heating stoves in indoor environments aggravate asthma symptoms in inner-city children, especially pre-school aged children. Nitrogen dioxide gas is most prevalent in industrial settings, but it also found at high levels in many poor, inner-city homes that have unvented gas stoves. In a recent report published in Environmental Health Perspectives, the Hopkins researchers report that asthma exacerbations were directly related to high concentrations of nitrogen dioxide in the inner-city homes they studied.

The research team compared the nitrogen dioxide levels in the homes of 150 inner-city Baltimore children aged 2-6 to the frequency and intensity of coughing, wheezing, shortness of breath, and chest tightness. Each 20-point increase in nitrogen dioxide levels led to 10 percent more days of coughing and 15 percent more days of limited speech due to wheezing. Eighty-three percent of the homes had gas cooking stoves and 72 percent were heated with natural gas. Forty-two percent of the households had annual incomes less than $25,000.

Asthma is the most common pediatric chronic disease affecting 6.2 million children in the United States alone. It is widely known that severe asthma is most prevalent in the inner-city environment. This is due in part to poor access to health care and environmental conditions such as the disproportionate exposure to indoor allergens, dust, cigarette smoke, and automobile exhaust. The authors conclude that physicians caring for children with asthma should ask about their home's heating and cooking appliances and recommend using alternatives if possible or at least encourage the parents to have the stoves properly vented.

Citation: Hansel NN, Breysse PN, McCormack MC, Matsui EC, Curtin-Brosnan J, Williams DL, Moore JL, Cuhran JL, Diette GB. A longitudinal study of indoor nitrogen dioxide levels and respiratory symptoms in inner-city children with asthma. Environ Health Perspect. 2008 Oct;116(10):1428-32.

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Particulate Air Pollution Can Alter the Electrical Functioning in the Heart

Frank E. Speizer, MD and Diane R. Gold, MD MPH
Harvard Medical School
P01ES009825 and P30ES000002

New research findings from NIEHS grantees at the Harvard University Department of Environmental Health suggests that exposure to fine particulate air pollution and black carbon particles can adversely effect the heart's ability to conduct electrical signals in people with pre-existing coronary artery disease. The study conducted with 48 Boston-area heart patients, found changes in the ST-segment of the patient's electrocardiograms, possibly indicating inadequate blood flow to the heart or inflamed heart muscle.

The average 24-hour levels for all pollutants measured in the study were below accepted National Air Quality standards indicating the patients were breathing air considered healthy. Fine particulate matter and black carbon are combustion by-products and are generated in areas of heavy traffic. The heart effects were highest within the first month after hospitalization, and for heart attack patients or those with

diabetes. Previous studies have shown an association between exposure to road traffic and heart problems.

All the patients had undergone in-hospital procedures to examine or open blocked coronary arteries. The ST-segment changes observed in the study were asymptomatic, but the findings expand the evidence that air pollution can affect heart health, either through inflaming the heart muscle or through reducing blood flow to the heart.

The American Heart Association and the American College of Cardiology recommend that some heart patients, particularly those who have had a heart attack, avoid driving for two to three weeks after leaving the hospital because of the stress heavy traffic can create. This study provides additional rationale to avoid or reduce heavy traffic exposure for people with heart conditions because of the potential exposure to elevated levels of air pollution particles. The study authors suggest additional research is necessary to determine whether the pollution-related ST-segment changes are due to increased heart inflammation, reduced blood flow, oxidative stress, or increased risk of arrhythmias.

Citation: Chuang KJ, Coull BA, Zanobetti A, Suh H, Schwartz J, Stone PH, Litonjua A, Speizer FE, Gold DR. Particulate air pollution as a risk factor for ST-segment depression in patients with coronary artery disease.Circulation. 2008 Sep 23;118(13):1314-20.

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Acetaminophen May Increase the Risk of Developing Asthma

Victoria Persky, MD
University of Illinois School of Public Health
R01ES011377

There is a growing body of scientific literature suggesting a causal link between the use of the non-steroidal anti-inflammatory drug acetaminophen and the rise in the incidence of asthma in children. A new epidemiologic study, supported by NIEHS, conducted with 345 pregnant women adds to the growing evidence.

There are plausible biological and associative links between acetaminophen and asthma. Acetaminophen became the drug of choice for pain and fever relief in the 1980s after several studies reported a link between Reyes syndrome and aspirin use. In 1986, the FDA placed warning labels regarding the Reyes Syndrome link on acetaminophen bottles. Shortly afterwards, pediatricians nationwide started noticing a rise in asthma incidence. Acetaminophen, unlike aspirin and ibuprofen, decreases the level of the antioxidant glutathione in the lungs and other tissues.

In the NIEHS-funded work, women were recruited during their first trimester of pregnancy. Use of acetaminophen during pregnancy was determined by a questionnaire and related to respiratory outcomes in their newborns during their first year of life. Use of acetaminophen in the second and third trimesters was significantly related to wheezing in the first year. While wheezing is a known symptom of asthma in young children, it alone does not constitute a diagnosis of asthma.

The findings in this report are consistent with previous literature showing increases in asthma symptoms after exposure to acetaminophen. The researchers will continue to follow these children until they reach 5 years of age enabling them to provide more precise estimates of asthma incidence. The researchers point out that this is only the second study suggesting that exposure to acetaminophen late in pregnancy may affect the subsequent development of allergic symptoms in the child. Confirmation of these finding in larger cohorts could have substantial public health implications in defining factors attributable to the development of asthma.

Citation: Persky V, Piorkowski J, Hernandez E, Chavez N, Wagner-Cassanova C, Vergara C, Pelzel D, Enriquez R, Gutierrez S, Busso A. Prenatal exposure to acetaminophen and respiratory symptoms in the first year of life. Ann Allergy Asthma Immunol. 2008 Sep;101(3):271-8.

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Green Tea Polyphenol Combats Health Effects of High Fat Diet
Chung S. Yang, Ph.D.
University of Medicine and Dentistry of New Jersey
P30ES005022

Green tea, consumed widely in East Asian countries, contains caffeine and polyphenolic compounds known as catechins. The most common catechin compound in green tea is epigallocatechin-3-gallate (EGCG). EGCG has been suggested as the catechin responsible for the potential health benefits experienced with long-term consumption of green tea.

A team of scientists at the University of Medicine and Dentistry of New Jersey with support from a NIEHS Center Grant has found that long-term treatment with EGCG reverses high-fat diet induced disorders in laboratory mice. In the study mice were fed a diet containing 60% of energy as fat for 16 weeks at which point some mice were given EGCG for another 16 weeks. Mice treated with EGCG had lower body weights, decreased insulin resistance, and lower plasma cholesterol than the untreated mice. EGCG treatment also decreased liver weight and liver triglycerides. Subsequent histological examination of liver tissue revealed decreased lipid accumulation in the liver cells of the treated mice. In another experiment, obese mice were given 4 weeks of EGCG treatment. These mice had decreased body fat and blood glucose as compared to the untreated controls.

These results indicate that physiological relevant doses of EGCG treatment can mitigate the development of obesity, symptoms of metabolic syndrome, and liver fat accumulation. The researchers conclude that these effects could be mediated by decreased fat absorption, decreased inflammation or other mechanisms. Further studies need to be carried out in humans to determine whether green tea or EGCG can be used to prevent the development of obesity and its adverse health outcomes.

Citation: Bose M, Lambert JD, Ju J, Reuhl KR, Shapses SA, Yang CS. The major green tea polyphenol, (-)-epigallocatechin-3-gallate, inhibits obesity, metabolic syndrome, and fatty liver disease in high-fat-fed mice. J Nutr. 2008 Sep;138(9):1677-83.

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A Fruit Fly Model for Amyotrophic Lateral Sclerosis
Bing Zhang, Ph.D.
University of Oklahoma
R21ES014441

A multi-university research team has developed a new laboratory model for studying the motor neuron disease amyotrophic lateral sclerosis (ALS). The researchers at the University of Oklahoma and the University of Pennsylvania created a transgenic fruit fly that is able to express human superoxide dismutase, an antioxidant enzyme that has been implicated in the hereditary form of ALS.

ALS is a progressive and fatal neurodegenerative disease of the motor nervous system. It is characterized by the loss of muscle function caused by dysfunction and death of motor neurons throughout the body. Ten to fifteen percent of ALS cases are considered to be of genetic origin. About one-fifth of hereditary ALS cases are linked to mutations in the gene encoding for superoxide dismutase. Uncovering how mutations in the enzyme lead to the dysfunction and death of motor neurons could illuminate how ALS develops and progresses in patients with both sporadic and hereditary forms of the disease.

In experiments using the new model, these researchers found that expression of the enzyme in the flies induced neurological damage along with accumulation of the enzyme in motor neurons accompanied by a stress response in the surrounding glial cells. This work suggests that superoxide dismutase can cause cell-autonomous damage to motor neurons. It also highlights the usefulness of the fruit fly model for studying ALS.

Citation: Watson MR, Lagow RD, Xu K, Zhang B, Bonini NM. A drosophila model for amyotrophic lateral sclerosis reveals motor neuron damage by human SOD1. J Biol Chem. 2008 Sep 5;283(36):24972-81.

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Arsenic and Type 2 Diabetes

Ana Navas-Acien, MD, Ph.D. and Ellen K. Silbergeld, Ph.D.
Johns Hopikins Bloomberg School of Public Health
P30ES003819

New research findings from the National Health and Nutrition Examination Survey suggest that exposure to levels of arsenic commonly found in drinking water may be a risk factor for type 2 diabetes. The findings suggest that millions of Americans may be at increased risk for type 2 diabetes based on the level of arsenic in their drinking water.

Data on the nearly 800 participants in the study for which urinary arsenic concentrations were available, indicated that urine levels of arsenic were significantly associated with the prevalence of type 2 diabetes. After splitting the subjects into 5 groups based on the level of arsenic in their urine, the researchers determined that those in the highest category were more than three and one-half times more likely to have diabetes. The strength of arsenic as a risk factor for diabetes is similar to other factors such as obesity.

Inorganic arsenic in drinking water at concentrations higher than 100 parts per million has been linked to type 2 diabetes in studies that took place in Taiwan, Mexico, and Bangladesh where drinking water is commonly contaminated with high levels of arsenic. The US drinking water standard is currently 10 parts per million, but most people on private wells have not had their water tested and aren't required to. The researchers estimate that about 13 million Americans live in areas where public water systems exceed the EPA standard for arsenic and this number does not included private wells and water systems.

Animal studies have shown that arsenic affects the production of glucose, insulin secretion and can cause insulin resistance. The current findings reinforce the need to evaluate the role of arsenic in diabetes development in prospective epidemiologic studies conducted in populations exposed to a wide range of arsenic levels.

Citation: Navas-Acien A, Silbergeld EK, Pastor-Barriuso R, Guallar E. Arsenic exposure and prevalence of type 2 diabetes in US adults. JAMA. 2008 Aug 20;300(7):814-22.

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Connection Between Built Environment and Obesity

Li Fuzhong, Ph.D.
Oregon Research Institute
R01ES014252

If you are a baby boomer living in a neighborhood with a high density of fast food restaurants, few sidewalks and no parks, you are more likely to be obese according to NIEHS-supported research conducted by the Oregon Research Institute. In contrast, people living in neighborhoods with higher mixed-land use, high street connectivity, better access to public transportation and more green and open spaces were more likely to engage in some form of neighborhood-based walking program.

This study was unique in that it focused on the baby boom population aged 50-75 which will become the major demographic group in healthcare utilization in the next 20 years. By 2030, 36 percent of the total US population will be over 50 as compared to 25 percent currently. Finding and ameliorating built environment limitations on physical activity are an important component in keeping this population healthy and reducing the health care burden.

Current estimates indicate that 34 percent of the US population aged 20 years or more are obese. The research findings point to the access to unhealthy food and lack of accessibility to spaces for exercise as contributing factors for the rise in obesity. The built environment can create barriers to exercise and existing recreational facilities. Simply encouraging people to eat better and get more exercise may not be enough. The researchers point out that zoning and development policies need to be altered to enable people to lead healthier lifestyles.

The researchers examined 120 neighborhoods in Portland, Oregon and more than 1,200 residents in these neighborhoods completed questionnaires providing basic demographic data along with information on exercise and eating habits.

Citation: Li F, Harmer PA, Cardinal BJ, Bosworth M, Acock A, Johnson-Shelton D, Moore JM. Built environment, adiposity, and physical activity in adults aged 50-75. Am J Prev Med. 2008 Jul;35(1):38-46.

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p53 Inhibits Cell Growth as well as Cell Proliferation

Michael Karin, Ph.D.
University of California San Diego
R01ES006376, R37ES004151, and P42ES010337

New research findings by NIEHS grantees at the University of California at San Diego that the tumor suppressor gene p53 is involved in regulating the growth of cells as well as the proliferation of cells. The p53 target genes that inhibit cell proliferation had long been known, but its targets for inhibiting cellular growth were unknown.

Abnormal cell proliferation and growth of cells are characteristics of cancer. The p53 protein acts in the cell nucleus to control the expression of other genes whose products can inhibit cell proliferation and growth. The researchers discovered that two p53 target genes, known as Sestrin1 and Sestrin2, provide an important link between p53 and a protein kinase called mTOR, a central regulator of cell size. Incidentally, mTOR is the target for the immunosuppressive drug rapamycin, which was recently shown to have anti-cancer activity.

The major tumor suppressor p53 can either inhibit cell proliferation and cell growth or induce cell death. Its different functions are mediated through numberous target genes and depend on the extent of damage to the cell. More than half of all human cancers are either missing p53 expression or express a defective version of the protein. Understanding the mechanisms by which p53 suppresses tumors may lead to the development of new cancer preventives and chemotherapeutic agents.

Citation: Budanov AV, Karin M. p53 target genes sestrin1 and sestrin2 connect genotoxic stress and mTOR signaling. Cell. 2008 Aug 8;134(3):451-60.

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The Ah Receptor is Essential for Mediating an Anti-Inflammatory Effect
B. Paige Lawrence, Ph.D. and Michael S. Denison, Ph.D.
University of Rochester and University of California Davis
R01ES0010619, K02ES012409, and R01ES012498

A research team made up of NIEHS grantees from the University of Rochester and the University of California at Davis has discovered a potentially new role for the Ah receptor in treating inflammatory or immunologic disorders. This research adds new information on the diverse functions of the receptor including xenobiotic metabolism, involvement in proper blood vessel formation, and now immune responses.

The team happened upon this discovery while investigating a low-molecular with compound with potent anti-inflammatory activity known as VAF347. The compound is a drug candidate which inhibits allergic lung inflammation. The team demonstrated that VAF347 interacts with the Ah receptor resulting in stimulation of its signaling pathway. Additional experiments in Ah receptor-deficient mice confirmed the connection. These mice are resistant to the compound's ability to block allergic lung inflammation. The data indicate the Ah receptor protein is an important target of VAF347 and its importance in mediating the anti-inflammatory effects of the compound.

Although the importance of the Ah receptor in mediating the toxicity of various organic compounds is well known, this finding suggests that harnessing the biological activity of the receptor for therapeutic purposes is possible and suggests a new tool for the treatment of inflammatory and immunologic disorders.

Citation: Lawrence BP, Denison MS, Novak H, Vorderstrasse BA, Harrer N, Neruda W, Reichel C, Woisetschläger M. Activation of the aryl hydrocarbon receptor is essential for mediating the anti-inflammatory effects of a novel low-molecular-weight compound. Blood. 2008 Aug 15;112(4):1158-65.

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PAPERS by DERT STAFF

Haugen, A.C., Goel, A., Yamada, K., Marra, G., Nguyen, T.P., Nagasaka, T., Kanazawa, S., Koike, Kikuchi, J., Zhong, X., Arita, M., Shibuya, K., Oshimura, M., Hemmi, H., Boland, R.C., Koi, M. Genetic instability caused by loss of MutS homologue 3 in human colorectal cancer. Cancer Research, October, 68, 8465-8472, 2008.

Bredemeyer AL, Helmink BA, Innes CL, Calderon B, McGinnis LM, Mahowald GK, Gapud EJ, Walker LM, *Collins JB*, Weaver BK et al: DNA double-strand breaks activate a multi-functional genetic program in developing lymphocytes. Nature 2008, 456(7223):819-823.

Galliher-Beckley AJ, Williams JG, *Collins JB*, Cidlowski JA: GSK-3{beta}-mediated Serine Phosphorylation of the Human Glucocorticoid Receptor Re-directs Gene Expression Profiles. Molecular and cellular biology 2008.

GRANTEE HONORS and AWARDS

Timothy D. Phillips, Ph.D., a professor of Toxicology in the Department of Veterinary Integrative Biosciences at Texas A&M University, was recently selected for the 2009 Walston Chubb Award for Innovation sponsored by the Sigma Xi Scientific Research Society. Sigma Xi, the international honor society of science and engineering, has nearly 60,000 members who were elected to membership based on their research potential or achievements. Sigma Xi presents the Walston Chubb Award for Innovation to honor and promote creativity in science and engineering. The award carries a $4,000 honorarium and an invitation to give the Walston Chubb Award Lecture at Sigma Xi's annual meeting. Dr. Phillips is the principal investigator on the Chemical Intervention Strategies project of the Texas A&M University Superfund Basic Research Program grant.

Bernhard Hennig, Ph.D., Program Director of the Superfund Basic Research Program at the University of Kentucky, has received a prestigious Fulbright Award to encourage collaborations between the University of Kentucky and the Universidad de Antioquia in Medellin, Colombia. Dr. Hennig will spend four months in Colombia during the spring of 2009, where he will teach a course in nutritional biochemistry and share his research expertise. The Fulbright Program is sponsored by the United States Department of State, Bureau of Educational and Cultural Affairs.

Eric Suuberg, Ph.D., Professor of Engineering and co-director of the Superfund Basic Research Program at Brown University, was awarded an honorary degree on September 17 by the Talliinn University of Technology (TUT) in Estonia. The honor recognized Suuberg's achievements in the fields of chemical engineering, fuel science, and environmental technology. The citation made special mention of Suuberg's "promotion of cultural contacts between Estonia and the United States, in particular scientific contacts between Tallinn University… and Brown University." Suuberg, of Estonian descent, has maintained strong professional ties to TUT for many years. In 2001 he was a Fulbright Scholar in Estonia, and he has served a lengthy term on the board of the Estonian-American National Council, which fosters cultural exchange between the United States and Estonia.

Sadis Matalon, Ph.D., Alice McNeal Professor of Anesthesiology, was named on July 3 as the director of the newly established Pulmonary Injury and Repair Center at the University of Alabama at Birmingham.

STAFF HONORS and AWARDS

Drs. Sally Eckert-Tilotta and Teresa Nesbitt, SRB; Drs. Gwen Collman and J. Patrick Mastin, OD; Drs. Cindy Lawler, Michael Humble and Frederick Tyson, COSPB; Dr. Christina Drew and Mr. Jerry Phelps, PAB; Drs. Kimberly Gray and Caroline Dilworth and Mr. Liam O'Fallon, SPHB; Mr. Joseph (Chip) Hughes and Ms. Sharon Beard, WETB; Ms. Beth Anderson, CRIS; and Ms. Carolyn Mason, GMB, received an NIH Merit Award "For superb teamwork in the conceptualization of the Partnerships for Environmental Public Health program."

Dr. Leroy Worth, Jr., SRB; Drs. Jerrold Heindel, Srikanth Nadadur and Frederick Tyson and Ms. Astrid Haugen, COSPB; Dr. David Balshaw, CRIS; Dr Kimberly McAllister, SPHB; Dr. J. Patrick Mastin, OD; Dr. Christina Drew, PAB; Dr. Bennett Van Houten, PAB/DIR; and Ms. Laurie Johnson and Mr. Michael Loewe, OM received an NIH Merit award "For exception service in the Institutes research efforts in Epigenomics."

Dr. Jerry Heindel, COSPB, and *Dr. Kimberly Gray, SPHB*, both received individual NIEHS Peer Awards at the annual awards ceremony in December "In Recognition for Outstanding Service."

Mr. Hughes, WETP, received an NIH Merit Award as part of the "DHHS Implementation Team for the Pandemic and All-Hazards Preparedness Act (PAHPA). This award was presented at the 2008 OD Honor Awards Ceremony on November 20 in the Natcher Auditorium, NIH in Bethesda, Maryland.

On August 14, EPA announced the 2007 Office of Research and Development awards. *Dr. Srikanth Nadadur, COSPB*, as a member of the Ozone and Lead Assessment Team, received the Bronze Medal for Commendable Service Award, "For outstanding, exceptional contributions in the completion of EPA's Air Quality Criteria for Ozone and Other Photochemical Oxidants and Air Quality Criteria for Lead." The award ceremony was held at the EPA campus in Research Triangle Park, North Carolina on September 17.

STAFF ACTIVITIES

Mr. Remington, WETP, presented on the "Roundtable on Chemical Emergency Preparedness: Key Issues on Safety & Health and Risk Communication" at a Public Health Preparedness Summit in San Diego, California on February 18-20.

Mr. Remington, WETP, presented at CDC's Communication Strategies for Addressing Radiation Emergencies and Other Public Health Crises Conference in Atlanta, Georgia on January 28-29.

Dr. Kirshner, COSPB, helped organize and participated in a workshop on "Drug abuse vulnerability and neurodevelopmental effect of early exposure to secondhand tobacco smoke: Methodological issues and research priorities?" on January 13 in Bethesda, Maryland.

Dr. Heindel, COSPB, was an invited speaker at the American Association of Intellectual and Developmental Disabilities Workshop at the Arlie Center in Warrenton, Virginia, December 11-12. The workshop was on "Toxic Chemicals and Vulnerable Populations: New Opportunities. He spoke on, "The Developmental Origins of Disease/Dysfunction: Environmental Exposures and Epigenetic Mechanisms." He also participated in a breakout session to develop a research agenda for the next five years in this area.

Dr. Henry, CRIS/SBRP, conducted two informational sessions at the SBRP Annual Meeting in Asilomar, California on December 8. "SBRP Training Network" outlined SBRP's efforts in linking student/postdoctoral trainees and tracking student successes; and "Early Career Funding Opportunities" highlighted NIEHS grants for young scientists.

Mr. Outwater, WETP, addressed the Advisory Board of the NIEHS funded University of Cincinnati Midwest Consortium on Jan 7 on the topic "NIEHS WETP Program Accomplishments."

Ms. Beard, WETP, participated in the EPA Brownfields Job Training Review Meeting in Philadelphia, Pennsylvania on December 8-10.

Dr. Henry, CRIS/SBRP, gave a presentation on "Environmental Benefits and Possible Risks of Engineered Nanomaterials" at the International Forum of EcoHealth meeting in Merida, Mexico on December 2nd. The talk featured SBRP and NIEHS research in nanotechnology device development, nanomaterials used for remediation, and toxicity studies.

Dr. Henry, CIRS/SBRP, moderated a session at the "Phytoremediation of Metals" web seminar broadcast through EPA's online training module CLU-IN.org on November 25. Part of a three-part series on phytoremediation, this session featured research by SBRP grantees demonstrating how plants can be used to remove or stabilize arsenic and other metals in soil. The series was sponsored by SBRP and an archive is available at:
http://www.niehs.nih.gov/research/supported/sbrp/events/riskelearning/phytoremediation.cfm.

Mr. Hughes and Mr. Remington, WETP, attended the International Association of Fire Fighters Instructors Development Conference in Charleston, South Carolina on November 12-14.

Drs. Collman, Maull, and Reinlib, SPHB, attended the annual business meetings of Breast Cancer and Environment Research Centers in Birmingham, Alabama, on November 11-12.

Dr. Heindel, COSPB, was an invited speaker at a meeting "Green Chemistry and Environmental Health: Problems Meet Solutions" held in Irvine. California, November 10. He spoke on "Endocrine Disruptors and Human Health."

Dr. Maull, SPHB, participated in the CounterACT-sponsored Sulfur Mustard Symposium in Albuquerque, New Mexico, November 5 – 7.

Mr. O'Fallon, SPHB, was invited to attend and participate in the November meeting of the U.S. EPA CARE grantees which was held in Chicago, Illinois. This year EPA and the CDC/ATSDR hosted a joint meeting of grantees with shared interests in community-based activities addressing environmental public health issues. As part of the three day meeting, the Federal partners had a meeting to discuss opportunities for

increased interactions. These agencies have been working together for the past year and have signed an MOU with regard to their environmental public health activities. Mr. O'Fallon was asked to present on the PEPH program and address ways in which NIEHS might be able to coordinate better with EPA and CDC/ATSDR. *Dr. Collman* participated in the meeting via phone. The presentation was well received and generated many questions as there are several shared areas of interest including a better coordinated web presence for environmental public health information. Mr. O'Fallon will arrange a presentation to this group on the NIH funding process.

Dr. Drew and Mr. Phelps, PAB, along with contract staff from the Battelle Centers for Public Health Research and Evaluation made presentations at the November 6-8 meeting of the American Evaluation Association in Denver, Colorado. Their session was entitled "Moving Beyond Bibliometric Analysis: Emerging Evaluation Approaches at the National Institute of Environmental Health Sciences. The presentations focused on the methods and results of a recently conducted evaluation of the NIEHS Asthma Research portfolio. The session was well attended and generated many positive responses among the evaluators in the audience. Note: A manuscript of the evaluation results has been submitted to EHP and is currently being revised after peer review.

Mr. Remington, WETP, presented at the National Response Team's Worker Safety Technical Conference, in Washington, DC on October 28-29

Ms. Beard, WETP, attended the 136th Annual American Public Health Meeting and Exposition in San Diego, California on October 27 and 29 where she presented "Training and Educating the Brownfields Workforce – the NIEHS Model at the session on Environmental Justice and Health Disparities at Brownfields Sites" and facilitated another session entitled "The Occupational Health Disparities Institute: Health and Safety for Latino/Hispanic Workers." She also participated in the session on "Labor Rights, Occupational and Environmental Health" on Saturday, October 25 at the San Diego City College hosted by the Environmental Health Coalition and the CITTAC – Information Center for Working Women and Men.

Dr. Henry, CRIS/SBRP, presented "A Diversity of Research Opportunities: NIEHS and SBRP," an informational session open to faculty, students, and the public given at Clemson University on October 21st. The talk outlined the breadth of research carried out under the SBRP and funding opportunities at NIEHS.

Dr. Humble, COSPB, participated in the Cell Biology and Cancer teacher workshop held at UNC-Chapel Hill on October 16th. The workshop was sponsored by the North Carolina Association for Biomedical Research (NCABR) and was attended by 20 North Carolina middle and high school science teachers. Dr. Humble was the moderator for the morning training session and introduced the cell biology and cancer curriculum and activities developed by NCABR and NIH.

NIEHS WETP hosted an awardee meeting, "Implications for Safety and Health Training in a Green Economy" in Chapel Hill, North Carolina on October 16-17. The meeting defined why and how green job training is important, and how green-collar jobs will be significant in developing the nation's new green economy. The WETP has an opportunity to develop and provide more courses on green concepts to workers, which will allow them to work more safely, productively, efficiently, and effectively in their jobs. To read the complete article on this meeting, please see: http://www.niehs.nih.gov/news/newsletter/2008/november/green-economy.cfm.

Dr. Heindel, COSPB, and Dr. Collman, OD, were invited participants at the Society of Environmental Journalists annual meeting in Roanoke Virginia October 15-19. Dr. Collman served on a panel titled "Does Environment Trump Genetics? Teasing out the Factors Affecting Women's Health." She also participated in a "beat" dinner with about a dozen reporters where she highlighted the NIEHS Partnerships for Environmental Public Health (PEPH) program. Dr. Heindel participated in a panel moderated by a reporter from the Milwaukee Journal Sentinel that focused on endocrine disruptors and toxicology. Heindel

also talked to reporters during a lunch session on how to communicate information about epigenetics to the general public.

Mr. Outwater, WETP, addressed the steering committee of the major DOE training facility in Hanford Washington Oct. 8-9, on "NIEHS Program Accomplishments." In attendance was U.S. Representative Doc Hastings.

Dr. Henry, CRIS/SBRP, chaired the "Nanotechnology-Enabled Sensors" session at the "International Environmental Nanotechnology" meeting in Chicago, Illinois on October 7. In addition to showcasing a variety of novel sensors, many designed for exposure assessment, the session also focused on maximizing positive impacts through green production and thorough life-cycle analyses.

Dr. Heindel, COSPB, was an invited speaker at The Obesity Society Annual Meeting, which was held in Phoenix, Arizona, October 3-7. His talk was "Obesity: Developmental Origins and Environmental Influences."

Ms. Beard, WETP, attended the North Carolina Central University sponsored conference on Growing a Just, Green Economy in Durham, North Carolina on September 20.

Ms. Beard, WETP, facilitated a panel on workforce development training at the Newark Green Future Summit in Newark, New Jersey, on September 12-13.

Mr. Hughes, Mr. Remington, and Mr. Outwater, WETP, conducted two sessions at the Department of Energy's (DOE) Integrated Safety Management conference in Idaho Falls, Idaho, on August 26. Each session focused on the NIEHS DOE program in relationship to new DOE worker safety regulations (CFR 851).

UPCOMING MEETINGS and WORKSHOPS

The 3nd Annual CounterACT Network Research Symposium will be held at the Omni Shoreham Hotel in Washington, DC, from April 14-16. This is an opportunity for the grantees of the CounterACT Program to share research findings related to the development of therapeutic countermeasures for chemical threats among the Network as well as develop future collaborations. *Dr. Elizabeth Maull, SPHB*, will be chairing the session on Pulmonary Agents. A poster networking session is included in the meeting, as well as a pulmonary pre-meeting workshop focused on chlorine exposures.

Dr. Carol Shreffler, COSPB, has organized an Education-Career Development session entitled, "The Future of Environmental Health Science: Featuring NIEHS funded Early Career Investigators," for the Society of Toxicology (SOT) Annual Meeting in Baltimore, Maryland, March 15-19. The session is scheduled to take place on Tuesday, March 17.

Drs. Srikanth Nadadur and Jerrold Heindel, COSPB, have organized an Education-Career Development session entitled, "Grantsmanship Forum: Tools and Skills needed to Navigate Toxicology Research Funding," for the Society of Toxicology (SOT) Annual Meeting in Baltimore, Maryland, March 15-19. The session is scheduled to take place on Monday, March 16.

The NIEHS WETP will cosponsor a grantee meeting and workshop, "Local, State and Federal Partnerships for Chemical Preparedness and Response," April 29-May 1 in Cincinnati, Ohio. The spring workshop will share knowledge, materials, and resources for chemical and all-hazards preparedness. It will also review a new draft training tool that addresses the health and safety hazards that response and recovery workers will face following a chemical incident.

STAFF CHANGES

Arrivals:
Dr. Lisa Helbling Chadwick joined COSPB as a Health Science Administrator on November 10. She received her B.A. in Biology from Case Western Reserve University. She received her Ph.D. in Genetics from Case Western Reserve University for her work in Dr. Huntington Ward's laboratory identifying genetic and epigenetic modifiers of X chromosome inactivation. Dr. Chadwick's scientific interests are primarily in mammalian genetics, epigenetics and chromatin biology. She came to DERT after completing a postdoctoral fellowship in Dr. Paul Wade's laboratory in the Laboratory of Molecular Carcinogenesis at NIEHS. Her postdoctoral research in Dr. Wade's laboratory focused on investigating a role for the Mi-2/NuRD chromatin remodeling complex in the heterochromatin assembly after DNA replication.

Ms. Jennifer Collins joined SPHB as a Program Analyst on September 28. She has a B.S. in Biological Sciences (2000) and a Master of Functional Genomics degree (2006) from North Carolina State University. Before joining the Division of Extramural Research and Training, Ms. Collins spent ten years in the Division of Intramural Research at NIEHS, primarily in the Microarray Core facility. As a biologist in this group, she was responsible for coordinating the collaborations between the core facility and intramural researchers and for conducting the initial analyses of all gene expression data generated in the lab. Jennifer is currently a program analyst in the Susceptibility and Population Health Branch in the Division of Extramural Research and Training. Her primary function is to assist in coordinating the activities related to the Exposure Biology Program of the Genes, Environment, and Health Initiative.

Ms. Helena Davis joined the Program Analysis Branch as a Program Analyst on February 1. She comes to DERT from The Smithsonian Institute.

Transfers:
Ms. Kathy Ahlmark transferred as a Program Analyst from the Superfund Basic Research Program to the Worker Education and Training Program in December.

Mr. James Williams transferred from his position as the DEAS Supervisor to the Grants Management Branch as a Grants Management Specialist on September 14.

Departures:
Ms. Susan Ricci departed GMB on January 17 to take a position as a budget analyst at Fort Stewart allowing her to join her new husband in Georgia.

Mr. Dwight Dolby retired from GMB on January 2.

COUNCIL DELEGATED AUTHORITIES AND GUIDELINES FOR STAFF ACTIONS

Introduction:

NIH Policy requires an annual review by Advisory Councils of the delegated authorities and operational guidelines under which institute staff operate. These guidelines fall into two general categories. First, Council-delegated staff actions are actions delegated to staff that require no follow up action with Council. Second, Council delegates to staff certain operational actions that are required to ensure the smooth operations of the extramural division in conducting business with our grantees; these actions require the establishment of a threshold level for Council involvement and are listed as section II.

Council-Delegated Staff Actions:

National Institute of Environmental Health Sciences (NIEHS) extramural staff may take the following actions without Council review.

1. Authorize relocation of a currently funded project to a new institution when the principal investigator transfers from one institution to another and the original grantee institution relinquishes the grant. Such projects may be supported at the new institution for a period of up to the remainder of the current project period and in an amount generally not to exceed that previously recommended for the remaining period.

This authorization also applies when the principal investigator moves to a new institution following concurrence with the Initial Review Group (IRG) action by Council, but prior to the time that an award is made.

2. Approve a new principal investigator or program director for a research grant or an institutional training grant, sub-project director or other key personnel on program projects or center grants, for a period equal to the time remaining on the current project. ~~Such changes involving directors of the University-based Environmental Health Sciences (EHS) Centers and Marine and Freshwater Biomedical Sciences (MFBS) Centers will be made in consultation with the Director, NIEHS.~~ *Recommend that this sentence be deleted.*

3. Extend a project grant period with additional funds to assure orderly termination of the project or to protect the investment already made.

Staff, in discussion with the principal investigator, will determine the period of support and budget necessary to permit orderly termination of the research project. Special attention will be given to salary for essential staff, for purchase of supplies and for support of experimental animals. The (prorated) supplemental award should not exceed 12 months.

In the case of training grants, stipends may be provided until completion of the training for those trainees already appointed to the program.

In cases where a competing renewal application is deferred by either the Initial Review Group (IRG) or the Council, or when bridging funds are needed until an amended application has been submitted funds may be provided to permit support of the previously recommended research until review is completed and a final decision on the competing renewal application has been made. If a competing award is made, interim funds and the period of support may be deducted from the budget and budget period of the first year of the continuation award.

4. Authorize supplemental funds in an amount not to exceed $50,000 direct costs (excluding consortium F&A costs) to any Center, program project, or other multi-disciplinary program grant or cooperative agreement for the purpose of supporting a conference, symposium or scientific workshop. This provision will apply in those instances in which the principal investigator or center director can show that the meeting is necessary for the scientific community or Institute.

5. Authorize supplemental direct cost funds to a Center in an amount not to exceed 15% of the direct costs (excluding consortium F&A costs) recommended for a current annual budget period. This provision will apply only in those circumstances where: 1) the Center Director can show adequate justification that such funds are required to cover unanticipated costs, or are needed to respond to newly identified problems of urgent program priority, or 2) the supplement is in response to special programmatic or budgetary needs or opportunities identified by the Director, NIEHS.

6. Authorize the award of funds ~~to research project grants, R25, and S11 grants~~ based on the receipt and approval of a supplemental application ~~to provide support for re-entry into research, disabled or under-represented minority investigators, under-represented minority undergraduate or graduate students to work on research aims previously reviewed during competitive evaluation of the parent grant~~ submitted in response to NIH Program Announcements on Research Supplements to Promote Diversity in Health-Related Research and Research Supplements to Promote Re-Entry into Biomedical and Behavioral Research Careers.

7. Authorize the award of supplemental funds when required to comply with emergency response needs as designated by specific appropriation language or as designated by the Director, NIEHS.

8. Approve continuation of grant under an interim principal investigator during the temporary absence of the principal investigator.

9. Approve extension, beyond the first extension, of grants without additional funds ~~on those grants requiring NIH approval~~. *Under the expanded authorities, the grantee institution has the authority to approve a one-time extension for up to 12 months time without additional.*

10. Take final action to increase ~~previously recommended and currently active research and~~ training grants ~~by the amount represented in institution-wide salary increases of grant-supported personnel or in~~ stipends of grant-supported trainees in accord with NIH

policy. *NIH began establishing total cost commitments for future years on all grants and cooperative agreement awards with budget period start dates after October 1, 1995. For this reason, ICs no longer provide additional support for increases in salary. Under expanded authorities, grantee institutions may rebudget to meet the increased salaries.*

~~11. Take final action to provide for the employer's portion of mandatory contributions required of employers in their locality when not included in the application and when requested subsequently.~~ *Unforeseen need covered under current number 13 below.*

~~12. Take final action to adjust grants to add summer salaries to current or renewal grants for which authorizing overall policy was adopted by the grantee institution subsequent to the filing of the application.~~ *Unforeseen need covered under current number 13 below.*

13. ~~Take final action to~~ provide supplemental ~~additional~~ funds not to exceed $150,000 direct costs (excluding consortium F&A costs) to ~~*research project grants, R25, and S11*~~ grants for increases in the budget for unforeseen needs ~~administrative costs of research~~ that are within the scope of the approved/funded project or protocol.

14. ~~Authorize the award of funds for an individual Fellowship based on the receipt of an application and peer review recommendation regardless of level of support.~~ *OER Policy Announcement 20072-01 states that "*Fellowship awards, however, are not required to undergo Advisory Council/Board review." *Since Council/Board review is not required, no Council delegated authority is needed.*

Reviewed and Approved by NAEHS Council on February 19, 2009

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Gwen Collman, Ph.D. 02/19/2008
Interim Director, DERT, NIEHS

NAEHS COUNCIL REVIEW OF GRANTS

I. Basis for Special Review of Individual Grant Applications:

Applications are presented to the National Advisory Environmental Health Sciences Council (NAEHS) for special consideration when:

1. The research proposed has been identified by either Council or staff as being of particular interest or concern;

2. Some aspect of the recommendation from the IRG has been questioned by either Council or staff, e.g., an apparent discrepancy between the comments in the summary statement and the percentile ranking/priority score;

3. Ethical, hazard, or safety issues or concerns are identified by staff;

4. Concerns about participation of human subjects are raised by the IRG or are identified by staff or Council, regardless of the percentile ranking/priority score;

5. Concerns are raised regarding the principal investigator's inclusion of minorities and women in study populations, regardless of the percentile ranking/priority score;

6. Concerns regarding the treatment of animals are raised;

7. The application is a reviewed foreign application with a fundable percentile ranking;

8. The application is a reviewed center grant application or supplement.

9. All reviewed program project and regular research grant applications with a ranking better than the 40th percentile or a priority score better than 250 and a budget in excess of $500,000 direct costs (excluding consortium F&A costs) in any one year will be identified by staff and may be raised for individual discussion by Council.

Applications not identified for individual discussion are reviewed en bloc.

II. Options for Council Action for Special Review:

The following options generally are available to the Council for each application that is identified for individual discussion.

1. Concurrence with the IRG scientific merit review;

2. Change in priority status to HPP (High Program Priority) or to LPP (Low Program Priority). An HPP designation elevates the relative funding position of an application but does not necessarily assure funding. An LPP designation lowers the relative funding position of an application, but does not necessarily prohibit funding. Staff will give special consideration to all HPP and LPP recommendations in making a final funding decision;

3. Deferral to NIEHS staff for additional information for Council consideration at a subsequent meeting;

4. Deferral for reconsideration of the scientific and technical merit of an application by the same or another IRG;

5. Non-concurrence with IRG recommendation for policy, procedure, or administrative reasons; or

In specific cases, additional options may be available. These will be detailed by the staff for the Council's consideration as the need arises.

III. Early Council Concurrence Using the Electronic Council Book:

The purpose of early Council concurrence is to expedite the funding of meritorious grant applications. It is anticipated that the time from submission of an application to eventual funding can be shortened by approximately one month. **The following information details the procedure for early Council concurrence:**

One or more subgroups of Council will be designated as participants in the early concurrence process. Each subgroup will be composed of three Council members with a broad range of expertise and experience. Members of the subcommittees will be solicited and confirmed at the **September/October Council meeting for the next calendar year.**

At least one month before the Council meeting, staff will identify applications for which there are no issues that would require special review requirements as indicated under item 1 above. These applications will be submitted to **the** subgroup electronically through the Electronic Council Book.

Council **subgroup** members will be notified electronically of the existence of the panel of applications and a "due date" for their action will be identified. **Subgroup** members may concur en bloc or may remove any or all applications from concurrence. Any application removed from the early concurrence process by **subgroup** members will be held for consideration at the Council meeting. Two of the three Council members on the subgroup are required for further staff action.

Upon early concurrence, as indicated above, staff may initiate the award process for meritorious applications within the pay line. All other applications will be considered at the Council meeting according to the procedures indicated above.

Reviewed and Approved by NAEHS Council on February 19, 2009

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Gwen Collman, Ph.D. 02/19/2009
Interim Director, DERT, NIEHS

NIEHS Awarded Competing Grants - Fiscal Year 2008

Principal Investigator	Grant Number	Grantee Institution	Project Title
Research Project Grants			
Abdel-Malek, Zalfa A.	2R01ES009110-10	University Of Cincinnati	Signaling Pathways for UV-Induced Melanogenic Response
Anger, Wyndham Kent	1R01ES016308-01	Oregon Health And Science University	Biomarkers of Organophosphorus Pesticide-Induced Neurotoxicity
Atchison, William D	2R01ES003299-19A2	Michigan State University	Neurotoxic Mechanism of Methylmercury Poisoning
Bain, Lisa J	1R15ES016640-01	Clemson University	Mechanisms of Arsenic-Induced Developmental Toxicity
Barchowsky, Aaron	1R01ES013781-01A2	University Of Pittsburgh At Pittsburgh	Mechanisms for Arsenic-Induced Vascular Disease
Belanger, Kathleen P.	1R01ES016317-01A1	Yale University	Effect of Air Pollution and Traffic on Birth Outcomes
Belinsky, Steven A	1R01ES015262-01A2	Lovelace Biomedical & Environmental Res	Genetic and Epigenetic Biomarkers for SCC of the Lung
Bellinger, David C	1R01ES016283-01	Children's Hospital Boston	Metal Exposure and Children?s Preschool Neurodevelopment
Ben-Jonathan, Nira Na	1R21ES016803-01	University Of Cincinnati	Exposure to Bisphenol A: Inhibition of Adiponectin Release by Human Adipocytes
Boone, Michelle Dawn	1R15ES016435-01	Miami University Oxford	Use of an Amphibian as an Alternative Model to Evaluate Effects of Contaminants o
Bornstein-Forst, Susan Meryl	2R15ES014355-02	Marian College Of Fond Du Lac	Physiological response of Escherichia coli to temperature and desiccation stress
Bowman, Aaron B	1R01ES016931-01	Vanderbilt University	Gene-environment interactions between manganese exposure and Huntington disease
Brouxhon, Sabine M	1R21ES015832-01A2	University Of Rochester	The role of E-cadherin in photocarcinogenesis
Brugge, Douglas M	1R01ES015462-01A1	Tufts University Boston	Community Assessment of Freeway Pollution and Health
Burchard, Esteban Gonzalez	1R01ES015794-01A1	University Of California San Francisco	Gene-environments and Admixture in Latino Asthmatics (GALA 2)
Campen, Matthew J	1R01ES014639-01A2	Lovelace Biomedical & Environmental Res	Enhancement Of Coronary Constriction By Combustion-Source Air Toxics
Carmichael, Suzan L	1R01ES017060-01	March Of Dimes Birth Defects Foundation	Genes, environmental exposures, and hypospadias
Carter, A Brent	1R01ES014871-01A2	University Of Iowa	Hydrogen Peroxide and Asbestosis
Chen, Jinbo	1R01ES016626-01	University Of Pennsylvania	Statistical Methods in Genetic Epidemiology Research
Chen, Yan-Hua	1R03ES016888-01	East Carolina University	Roles of Claudin-7 in Lung Cancer
Chesselet, Marie-Francoise	1P01ES016732-01	University Of California Los Angeles	Center for Gene Environment in Parkinson's Disease
Chusuei, Charles	2R15ES012167-02A1	University Of Missouri-Rolla	Role of Selenocystine in Lead Toxicity
Cimprich, Karlene A	1R21ES016867-01	Stanford University	Identifying Novel Mechanisms and Regulators of Genome Stability
Cockburn, Myles G	1R01ES015552-01A1	University Of Southern California	Defining critical aspects of environmental ultraviolet exposure in melanogenesis
Culotta, Valeria C	2R01ES008996-11	Johns Hopkins University	Intracellular Pathways of manganese Trafficking
Das, Sanjoy Kumar	2R01ES007814-09A1	Children's Hospital Med Ctr (Cincinnati)	Environmental Toxins and Uterine Gene Expression
Davidson, Philip W	1R21ES015487-01A1	University Of Rochester	Autism in a Fish Eating Population
Dawson, Douglas A	2R15ES008019-04	Ashland University	Mixture Toxicity - Evaluation of an Improved Methodology
Dobrinski, Ina	1R21ES014856-01A2	University Of Pennsylvania	Effect of chronic low-dose phthalate exposure on the immature primate testis
Doetsch, Paul W	2P01ES011163-06A1	Emory University	Cellular Responses to Oxidative Stress in Models of Colon Cancer Development
Dong, Zigang	1R01ES016548-01	University Of Minnesota Twin Cities	The role of histone phosphorylation in arsenic-induced cell transformation and sk
Doorn, Jonathan A	1R01ES015507-01A1	University Of Iowa	Organochlorine-Mediated Generation of a Dopamine Derived Neurotoxin
Essigmann, John M	1R01ES016313-01	Massachusetts Institute Of Technology	The Environment as a Variable to Calibrate Mouse Models of Human Disease
Farmer, Patrick J	1R21ES016441-01	University Of California Irvine	Nitroxyl adducts as structural probes of oxygenase/substrate interactions
Field, Jeffrey M	1R01ES015662-01A2	University Of Pennsylvania	Mutagenesis of p53 by reactive PAH and ROS
Fitsanakis, Vanessa A	1R15ES015628-01A1	King College	Neurotoxicity of Maneb and Roundup
Foster, W Michael	1R01ES016347-01A1	Duke University	Dependency of O-3 Induced Lung Mucus Hypersecretion on NQ01
Foster, W Michael	1R21ES016659-01A1	Duke University	Functional implications of the TNF
Fruin, Scott Anthony	1R21ES016986-01	University Of Southern California	Remote Sensing of Wildfire Smoke Exposures to Assess Health Effects
Fuentes, Montserrat	1R01ES014843-01A2	North Carolina State University Raleigh	A Spatial-Temporal Modleing Approach for Environmental Epidemiological Data
Gelineau-Van Waes, Janee	1R21ES016382-01A2	University Of Nebraska Medical Center	Material Fumonisin Exposure and Pregnancy Outcome: Decoding the Sphingolipid Immu
Gershon, Robyn R	1R21ES015347-01A2	Columbia University Health Sciences	Noise Exposure in Subway Riders
Ghribi, Othman	1R01ES014826-01A2	University Of North Dakota	Cholesterol induces oxidative stress and triggers iron and A? accumulation
Glazer, Peter M	2R01ES005775-16	Yale University	Hypoxia, Genetic Instability and DNA Mismatch Repair

Principal Investigator	Grant Number	Grantee Institution	Project Title
Research Project Grants (Continued)			
Goodman, Myron F	2R01ES012259-19	University Of Southern California	Biochemical Basis of SOS-Induced Mutagenesis
Groopman, John D	2P01ES006052-15A1	Johns Hopkins University	Molecular Biomarkers For Environmental Toxicants
Guilarte, Tomas R	2R56ES010975-06A1	Johns Hopkins University	Molecular & Behavioral Effects of Low Level Mn Exposure
Halpert, James R	2R01ES003619-26A1	University Of California San Diego	Molecular Basis of Selective P450 2B Function
Hammond, S Katharine	1R01ES014049-01A2	University Of California Berkeley	Neurologic and Reproductive Effects of Hexane on Workers
Hansel, Nadia N	1R21ES015781-01A1	Johns Hopkins University	Domestic endotoxin exposure and chronic obstructive pulmonary disease
Hansen, Laura A	1R01ES015585-01A1	Creighton University	Mechanisms of UV-induced skin carcinogenesis
Haynes, Erin N	1R01ES016531-01	University Of Cincinnati	Marietta Community Actively Researching Exposure Study
Heggland, Sara Jane	1R15ES015866-01A1	Albertson College Of Idaho	Mechanisms of Cadmium-induced Osteotoxicity
Hollingsworth, John W	1R01ES016126-01A1	Duke University	Ozone Primes Pulmonary Innate Immunity
Khan, M. Firoze	1R01ES016302-01	University Of Texas Medical Br Galveston	Oxidative Stress and Autoimmunity
Komuro, Hitoshi	1R01ES015612-01A2	Cleveland Clinic Lerner Col/Med-CWRU	Effects of Methylmercury on Neuronal Cell Migration
Kordas, Katarzyna	1R21ES016523-01	Pennsylvania State University-Univ Park	Nutritional and Heavy Metals: Effects on Child Learning and Behavior in Uruguay
Kumar, Naresh	1R21ES014004-01A2	University Of Iowa	Mortality and Air Quality Regulation in Two Indian Cities
Laden, Francine	1R01ES016284-01A1	Brigham And Women'S Hospital	Biomarkers Of Exposure And Effect In A Traffic Exposed Population
Ladiges, Warren C.	1R21ES016572-01	University Of Washington	Cancer susceptibility of XRCC1 mutant mice
Laskin, Debra Lynn	2R01ES004738-16A2	Rutgers The St Univ Of Nj New Brunswick	Activated Macrophages and Ozone Toxicity
Lee, Marietta Y.	1R01ES014737-01A2	New York Medical College	Modification of DNA Polymerase Delta by a Novel Mechanism During Replication Stre
Li, Lian	1R01ES015813-01A1	Emory University	Pathogenic Mechanisms of Environmental Toxicants in Parkinson's Disease
Lin, Anning	1R01ES015868-01A1	University Of Chicago	Wiring the UV Signaling Circuitry
Lipton, Stuart A	1P01ES016738-01	Burnham Institute For Medical Research	La Jolla-Parkinson's Disease Center Grant
Loch-Caruso, Rita K	1R01ES014860-01A2	University Of Michigan At Ann Arbor	Mechanisms of Inflammation in Gestational Membranes
Lopachin, Richard Michael	2R01ES003830-21A1	Montefiore Medical Center (Bronx, Ny)	The Nerve Terminal as the Site of Action for Type-2 Alkenes
Lu, Yi	1R01ES016865-01	University Of Illinois Urbana-Champaign	Selection, Characterization & Application of Paramagnetic Metal-specific DNAzymes
Malkova, Anna L	1R03ES016434-01	Indiana Univ-Purdue Univ At Indianapolis	Visualization of break-induced replication.
Manatunga, Amita K	2R01ES012458-05	Emory University	Analytical Methods: Environmental/Reproductive Epidemiology
Martin, David Ik	1R21ES016581-01	Children's Hospital & Res Ctr at Oakland	An Assay to Identify and Classify Epimutagens
Mcconnell, Rob S	1R01ES016535-01	University Of Southern California	Childhood Asthma, Susceptibility and Biological Activity of Ambient Particles
Mcilvane, William J	1R21ES015464-01A1	Univ Of Massachusetts Med Sch Worcester	Translational Studies of Neurobehavioral Effects of Mercury Exposure
Midoro-Horiuti, Terumi	1R21ES016428-01	University Of Texas Medical Br Galveston	Perinatal exposure to environmental estrogens and asthma pathogenesis
Miller, Gary W	1P01ES016731-01	Emory University	Emory Parkinson's Disease Collaborative Environmental Research Center
Money, Nicholas P	1R15ES016425-01	Miami University Oxford	Spore Release Mechanisms in Indoor Fungi
Mu, Fangping	1R21ES016920-01A1	Los Alamos Nat Secty-Los Alamos Nat Lab	Predicting Reactions of Xenobiotic Compounds in Mammals
Mustacich, Debbie J	1R21ES015872-01A1	Oregon State University	Prophylactic Use of Vitamin E for Prevention of Occupational PAH-Induced Damage
Nathanson, Neil Marc	1R01ES015594-01A2	University Of Washington	Organophosphate Action in the Central Nervous System
Nebert, Daniel W.	1R21ES015335-01A1	University Of Cincinnati	Genetic Differences in PCB-Induced Behavior
Nel, Andre E.	1R01ES016746-01	University Of California Los Angeles	Nano-Biological Interactions and Toxicity of Engineered Metal Oxide Particles
Newschaffer, Craig J	1R01ES016443-01	Drexel University	Early Autism Risk Longitudinal Investigation (EARLI) Network
Oken, Emily	1R01ES016314-01	Harvard Pilgrim Health Care, Inc.	Effects of prenatal diet and mercury exposure on child behavior and development
O'Neill, Marie Sylvia	1R01ES016932-01	University Of Michigan At Ann Arbor	Air Pollution, Inflammation and Preterm Birth: A Mechanistic Study in Mexico City
Ortiz, Luis A.	2R01ES010859-07A1	University Of Pittsburgh At Pittsburgh	TNF-alpha Signaling in Silica-induced Lung Fibrosis
Padmanabhan, Vasantha	1R56ES016541-01	University Of Michigan At Ann Arbor	Bisphenol-A and the Reproductive Dysfunction
Philbert, Martin A	2R01ES008846-08A2	University Of Michigan At Ann Arbor	Role of Astrocyte Injury in Neuroprotection
Pi, Jingbo	1R01ES016005-01A1	The Hamner Institutes	Paradoxical roles of Nrf2 activation in arsenic-induced beta-cell dysfunction
Pinney, Susan Mengel	1R21ES017176-01	University Of Cincinnati	Exposure Biomarkers of Polyfluoroalkyl Compounds in Persons Living in the Ohio Ri

Principal Investigator	Grant Number	Grantee Institution	Project Title
Research Project Grants (Continued)			
Pollard, Kenneth Michael	1R01ES014847-01A2	Scripps Research Institute	Role of Daf in Systemic Autoimmunity
Porter, Ned A	2P01ES013125-04	Vanderbilt University	Lipid Peroxidation and Antioxidant Mechanisms
Prakash, Louise	2R01ES012411-06	University Of Texas Medical Br Galveston	Translesion DNA synthesis in humans
Prakash, Satya	1R01ES016666-01A2	University Of Texas Medical Br Galveston	Role of Rev1 in error-free replication of DNA damage and in mutation prevention
Prins, Gail S	1R01ES015584-01A1	University Of Illinois At Chicago	Epigenetic Basis for Prostate Carcinogenesis following Early Estrogenic Exposures
Puett, Robin	1R03ES016619-01	Harvard University (Sch Of Public Hlth)	Particulate Exposure and Cardiovascular Disease in the HPFS
Runge-Morris, Melissa A	2R01ES005823-15A2	Wayne State University	Sulfotransferase Expression: Implications for Toxicity
Rusyn, Ivan	1R01ES015241-01A1	University Of North Carolina Chapel Hill	Bioengineering partnership to improve chemical hazard testing paradigms
Sagiv, Sharon K	1R03ES016604-01A1	Harvard University (Sch Of Public Hlth)	Prenatal Exposure To Methylmercury And Childhood Behavior
Schneider, Jay S	1R01ES015295-01A2	Thomas Jefferson University	Environment and Gene Effects on Brain and Behavior
Schwander, Stephan K	1R21ES016928-01	Univ Of Med/Dent Of Nj-Nj Medical School	Diesel Exhaust Particle Effects on Human Immunity to Mycobacterium tuberculosis
Schwartz, Joel D	1R01ES014663-01A2	Harvard University (Sch Of Public Hlth)	Cardiovascular Effects of Particles:The Role of Oxidative Stress and Metal Pathw
Sheikh, M Saeed	1R21ES016668-01	Upstate Medical University	Characterization of a novel stress-regulated anti-apoptotic ubiquitin ligase
Sheng, Shaohu	1R01ES014701-01A2	University Of Pittsburgh At Pittsburgh	Epithelial Sodium Channels and Pulmonary Toxicity of Zinc
Shi, Xianglin	1R01ES015518-01A1	University Of Kentucky	Reactive oxygen species in Ni(II) carcinogenesis
Slitt, Angela L	1R01ES016042-01A1	University Of Rhode Island	Effect of nutritional status on MRP2 expression and biliary excretion of bispheno
Sonenshein, Gail E	2P01ES011624-06A1	Boston University Medical Campus	Signaling Pathways in Stages of Tumorigenesis
Stapleton, Heather M	1R01ES016099-01A1	Duke University	Children's Exposure to Flame Retardants: Effects on Thyroid Hormone Regulation
States, J.Christopher	1R21ES015812-01A1	University Of Louisville	Transplacental Arsenic Induced Hepatic Dysfunction and Vascular Disease
Stein, T Peter	1R01ES015316-01A2	Univ of Med/Dent NJ-Sch of Public Health	Phthalate Exposure and Pregnancy Outcome
Styblo, Miroslav	1R01ES015326-01A2	University Of North Carolina Chapel Hill	Environmental arsenic and diabetes mellitus
Tanguay, Robert L	1R01ES016896-01	Oregon State University	Defining nanomaterial-biological interactions to enhance biocompatibility and bio
Thiruchelvam, Mona	1R01ES016277-01	Univ of Med/Dent NJ-R W Johnson Med Sch	Developmental Pesticide Exposure: The Parkinson's Disease Phenotype
Tielsch, James M	1R01ES015558-01A2	Johns Hopkins University	Cookstove Replacement for Prevention of ARI and Low Birthweight in Nepal
Townsend, Craig A	2R01ES001670-30	Johns Hopkins University	Aflatoxin Biosynthesis and Iterative Type I Polyketide Synthases
Tsao, Hensin	1R21ES013964-01A1	Massachusetts General Hospital	The Role of EphA2 in UV-mediated Apoptosis
Vandevoort, Catherine A	1R01ES016770-01	University Of California Davis	Effects of Fetal Bisphenol A Exposure on Oogenesis in Primates
Vaziri, Cyrus	1R01ES016280-01A1	Boston University Medical Campus	A Novel Role for the Fanconi Anemia Pathway in Replication of B[a]P-Adducted DNA
Walker, Cheryl L	2R01ES008263-10A1	University Of Texas Md Anderson Can Ctr	Environmental Estrogens and Uterine Leiomyoma
Waller, Lance A	1R01ES015525-01A1	Emory University	Spatial Statistics for Disease Ecology
Walther, Frans J.	1R01ES015330-01A2	La Biomed Res Inst/ Harbor Ucla Med Ctr	Synthetic surfactant and toxic chemical lung injury
Ward, Anthony John	1R01ES016336-01	University Of Montana	Indoor woodsmoke PM and asthma: a randomized trial
Webster, Thomas F	1R01ES015829-01A1	Boston University Medical Campus	Measuring Human Exposure to PBDEs
Wei, Qingyi	2R01ES011740-06A2	University Of Texas Md Anderson Can Ctr	Molecular Epidemiology of DNA Repair in Head and Neck Cancer
Wilson, Glenn L	2R01ES003456-22A2	University Of South Alabama	Environmental Beta Cell Toxins - Mechanisms of Action
Wood, David W	1R21ES016630-01	Princeton University	Bacterial Biosensors for Endocrine Disrupting Compounds
Wu, Jun	1R21ES016379-01A1	University Of California Irvine	Exposure to mobile source air pollution and adverse birth outcomes in the Los Ang
Wu, Tiejian	1R03ES016368-01	East Tennessee State University	Effects of Personal Exposure to Volatile Organic Compounds on Liver Function
Xia, Zhengui	1R01ES013696-01A2	University Of Washington	Pesticides and Parkinson's Disease
Yadav, Jagjit S	1R01ES015543-01A1	University Of Cincinnati	Fungal P450 Systems In Biodegradation Of Higher Pahs-R01Es15543-01
Yantasee, Wassana	1R21ES015620-01A1	Battelle Pacific Northwest Laboratories	Novel Chelators for Highly Efficient Removal of Toxic Heavy Metals in Humans
Zawia, Nasser Hussein	1R56ES015867-01A1	University Of Rhode Island	Occupational exposure and the developmental-basis of AD
Zhang, Junfeng	1R01ES015864-01A1	Univ of Med/Dent NJ-Sch of Public Health	Responses to Drastic Changes in Air Pollution: Reversibility and Susceptibility

Principal Investigator	Grant Number	Grantee Institution	Project Title
SBIR/STTR Grants			
Birks, John W	1R43ES016925-01	2B Technologies, Inc.	Personal Ozone Monitor
Bolduc, Elroy J.	1R43ES016474-01	Athena Group, Inc.	Teacher's iPod
Chandrasekhar, Prasanna	2R44ES013803-02A2	Ashwin-Ushas Corporation, Inc.	Microwave Remediation Of Hazardous Medical Wastes
Dertinger, Stephen D	2R44ES015940-02	Litron Laboratories, Ltd.	Versatile Mutation Assay Based on the Pig-A Locus
Gibson, Walter M	1R43ES016689-01	X-Ray Optical Systems, Inc.	Analyzer for Monitoring Personal Environmental Exposure to Fluids and Materials
Glaser, Jacob R	1R43ES017180-01	Microbrightfield, Inc.	System for comprehensive tracking and analysis of C. elegans behaviors
Goswami, Kisholoy	2R44ES012553-02A1	innosense, LLC	Sensitive To Low Ppm And Reversible Sensor For Co
Hering, Susanne V	2R44ES014997-02	Aerosol Dynamics, Inc.	A Miniature Monitor for Time-Resolved Airborne Particle Chemistry
Jackson, George W	1R41ES016478-01	Biotex, Inc.	In vivo Selection of Ribosomal Aptamers for Improved Bioremediation
Kaluzhny, Yulia	1R43ES017178-01	Mattek Corporation	In Vitro Assay to Determine Skin Corrosivity Packing Groups
Kostelecky, Clayton J.	1R43ES017192-01	Synkera Technologies, Inc.	Nanostructured Electrochemical Ozone Monitors
Laiz, Jacqueline H	1R43ES016964-01	Plastipure, Inc.	Estrogen Free Polymer Formulations for Food Packaging and Baby Products
Lee, David A	1R43ES016482-01	Edenspace Systems Corporation	Development of Enhanced Plants for Remediation of Cadmium and Lead
Li, Chunqi	9R44ES017366-02	Phylonix Pharmaceuticals, Inc.	Phase 2 SBIR: Zebrafish Cytochrome P450 Assays for Assessing Drug Metabolism and
Lu, Yi	2R42ES014125-02A2	Dzymetech, Inc.	Catalytic DNA Biosensor for Toxic Metal Ions
Mapes, James Preston	1R43ES016720-01	Rules-Based Medicine, Inc.	Biomarker Profiles for Carbon Monoxide Poisoning
Mcelaney, Lisa A	2R44ES014495-02	Vida Health Communications, Inc.	Managing Environmental Risks in Pregnancy
Nagarkar, Vivek V	2R44ES012361-03A1	Radiation Monitoring Devices, Inc.	A New High Performance Detector for Small Animal SPECT
Patel, Sanjay V	1R43ES016941-01	Seacoast Science, Inc.	Low-Cost Electronic Nose for Groundwater Contaminants
Polyakov, Oleg G	1R43ES016685-01	Synkera Technologies, Inc.	Formaldehyde Molecular Recognition Microsensor
Recio, Leslie	1R43ES016700-01	Integrated Laboratory Systems, Inc.	Validation Of A Human Cd34+ Stem Cell Toxicity Bioassay
Schantz, Hans Gregory	1R41ES016727-01	Q-Track Corporation	Location Aware Radiation Monitoring System
Su, Xiao-Li	1R43ES016699-01	Biodetection Instruments, LLC	Monolithic Reagentless Biosensor for Online Monitoring of Waterborne Pathogens
Su, Xiao-Li	1R43ES016704-01	Biodetection Instruments, LLC	A Microfluidic Biochip for Rapid Screening of Pesticide Residues
Thompson, Clay	2R42ES014137-02	Blueingreen, LLC	Point Source Ozonation to Minimize Antibiotic Resistance
Wisnewski, Adam	1R41ES016728-01	L2 Diagnostics, LLC	New Serodiagnostics for Isocyanate Exposure, A Major Cause of Occupational Asthma
Research Center Grants			
Groopman, John D	2P30ES003819-21	Johns Hopkins University	Johns Hopkins Center in Urban Environmental Health
Ho, Shuk-Mei	2P30ES006096-16A1	University Of Cincinnati	Environmental Genetics
Kaufman, Joel D	1P50ES015915-01	University Of Washington	DISCOVER Center: Cardiovascular Disease and Traffic-Related Air Pollution
Santella, Regina M	2P30ES009089-10	Columbia University Health Sciences	Center for Environmental Health in Northern Manhattan

Principal Investigator	Grant Number	Grantee Institution	Project Title
Other Research Grants			
Baker, Dean B.	1R13ES016969-01	University Of California Irvine	2008 Joint Annual Conference of the International Society for Environmental Epide
Ballatori, Nazzareno	1R25ES016254-01	Mount Desert Island Biological Lab	MDIBL STEER: Pathways of Chemical Action in Human Disease
Brisson, Jennifer A	1K99ES017367-01	University Of Southern California	Contrasting environmental and genetic controls of alternative phenotypes
Cheng, Xiaodong	1R13ES016695-01	Federation Of Amer Soc For Exper Biology	2008 FASEB Summer Research Conference on Biological Methylation: from DNA to Hist
Collins, Michael D	1R13ES016930-01	Teratology Society	Teratology Society 48th Annual Meeting: Student and Postdoctoral Travel Awards
Cooper, Priscilla K	1R13ES017216-01	Environmental Mutagen Society	Environmental Mutagen Society 48th Annual Meeting
Crank, Keith N	1R13ES016916-01	American Statistical Association	Conference Support for the 2008 Biannual Conference on Radiation and Health, "New
Cranmer, Joan Marie	1R13ES017188-01	University Of Arkansas Med Scis Ltl Rock	Environmental Etiologies of Neurological Disorders: Scientific, Translational and
Dong, Zigang	1R13CA135806-01	University Of Minnesota Twin Cities	2008 International Symposium
Ettinger, Adrienne S	1K01ES014907-01A1	Harvard University (Sch Of Public Hlth)	Genetic & Epigenetic Modifiers of Maternal-Fetal Transfer of Toxicants & Outcomes
Fuchs-Young, Robin S.	1R25ES016147-01	University Of Texas Md Anderson Can Ctr	EHS Summer Undergraduate Research Program (EHS-SURP)
Holian, Andrij	1R25ES016247-01	University Of Montana	Careers in Environmental Health Through Summer Research Experiences
Jenny, Matthew J	1K99ES017044-01	Woods Hole Oceanographic Institution	Metal-Regulatory Factor 1 (MTF-1) Role in Development and Stress Response
Kalman, David A	1R25ES016150-01	University Of Washington	Undergraduate Summer Research Experience in Environmental Health Sciences
Laiosa, Michael	1K99ES016585-01	University Of Rochester	Environmental Influence on T-Cell Leukemia: Role of Notch and AhR Signaling
Li, Lei	1K99ES017177-01	University Of Michigan At Ann Arbor	Enzyme Catalysis of Toluene Degradation and Unusual DNA Photoproduct Repair
Lund, Amie K	1K99ES016586-01	Lovelace Biomedical & Environmental Res	MMP-9 Activity Mediates Vascular Effects of Inhaled Environmental Air Pollutants
Maizels, Nancy	1R13CA134025-01	Gordon Research Conferences	Mutagenesis 2008 Gordon Research Conference
Mccauley, Linda A.	1R25ES016146-01	University Of Pennsylvania	Summer Mentorship in Environmental Health Sciences for High School and Undergradu
Mccormack, Meredith	1K23ES016819-01	Johns Hopkins University	The Impact of Indoor Particulate Matter Exposure on Non-Allergic Asthma
Miller, Marion G	1R25ES016249-01	University Of California Davis	Short Term Educational Experiences for Research (STEER) in Environmental Health S
Mitra, Sankar	1U13CA136020-01	University Of Texas Medical Br Galveston	3rd US/EU Conference on Repair of Endogenous Genome Damage
O'Brien, Karen	1R13ES016981-01	Virgina Organizing Project	Forging Synergies Between Environmental Health and Green Chemistry
Pitt, Bruce R	1R25ES016148-01	University Of Pittsburgh At Pittsburgh	University of Pittsburgh: Short-Term Educational Experiences for Research (PITT-S
Robertson, Andrew D	1R13ES016960-01	Keystone Symposia	Epigenetics, Development and Human Disease
Robertson, Andrew D	1R13ES017382-01	Keystone Symposia	Frontiers in Reproductive Biology and Regulation of Fertility
Salahpour, Ali	1K99ES016816-01	Duke University	Toxicant evaluation in mice with selective dopamine transporter overexpression
Schantz, Susan L	1R13ES016690-01	University Of Illinois Urbana-Champaign	Neurobehavioral Teratology Society: Symposium on Pesticides and Metals
Sens, Donald A	1R25ES016250-01	University Of North Dakota	Steering Undergraduate Interest in Environmental Health Sciences at the Universit
Smith, Susan M.	1R13DK081216-01	Federation Of Amer Soc For Exper Biology	14th Biennial FASEB Summer Research Conference on Retinoids
Sobol, Robert W	1R13ES016721-01	University Of Pittsburgh At Pittsburgh	Annual Midwest DNA Repair Symposium
Spanier, Adam J	1K23ES016304-01	Children's Hospital Med Ctr (Cincinnati)	Prenatal Low Level Tobacco & Phthalate Exposure & Childhood Respiratory Health
Spear, Robert C	1R25ES016252-01	University Of California Berkeley	Summer Training Program in Environmental Health Sciences for High School and Unde
Stanton, Mark E.	1R13HD059279-01	University Of Delaware	NBTS Symposium: Fetal Behavior and Neurotoxicology
Stegeman, John J	1R13ES016678-01	Gordon Research Conferences	2008 Oceans and Human Health Gordon Research Conference
Stone, Michael P	1R13ES016957-01	Vanderbilt University	ACS Symposium, Frontiers in Chemical Toxicology
Summers, Anne O	1R13ES016679-01	Gordon Research Conferences	Environmental Bioinorganic Chemistry 2008 Gordon Research Conference
Sun, Qinghua	1K01ES016588-01	Ohio State University	Air Pollution and Microvascular Dysfunction: Leukocyte-Dependent NAD(P)H Oxidase
Swan, Shanna H	1R13ES016703-01	Gordon Research Conferences	Environmental Endocrine Disrupters 2008 Gordon Research Conference
Tang, Wan Y	1K99ES016817-01	University Of Cincinnati	Estrogens/Xenoestrogens and Epigenetic Regulation of Gene Expression
Trush, Michael A	1R25ES016149-01	Johns Hopkins University	Connecting Students to Environmental Health Research
Vlahov, David H	1R13ES017205-01	New York Academy Of Medicine	7th International Conference on Urban Health
Vore, Mary E.	1R25ES016248-01	University Of Kentucky	Summer Education Experience for Research
Wright, Peter Edwin	1R13GM084505-01	Scripps Research Institute	International Conference on Magnetic Resonance in Biological Systems 2008

Principal Investigator	Grant Number	Grantee Institution	Project Title
Individual Research Training Grants			
Englert, Judson M	1F30ES016973-01	University Of Pittsburgh At Pittsburgh	A Role for Advanced Glycation End-Products in Diabetic Lung Injury
Geddie, Melissa L	1F32ES016493-01	Whitehead Institute For Biomedical Res	Metal Ion Transport in Parkinson's Disease
King Heiden, Tisha C	1F32ES016714-01	University Of Wisconsin Madison	Early life stage exposure to TCDD produces persistent, heritable cardiac toxicity
Kung, Vanderlene L	1F30ES016487-01	Northwestern University	Pseudomonas aeruginosa genomic islands and virulence factors
Mullen, Thomas D	1F30ES016975-01	Medical University Of South Carolina	Ceramide Synthases CERS5 and CERS6 Regulate Pathways of Programmed Cell Death
Potts, Rebekah G	1F30ES016488-01	University Of North Carolina Chapel Hill	Antiobic Resistance and Virulence Gene Transfer in Environmental Pathogens
Rogers, Erica N	1F31ES016719-01	University Of Louisville	Curcumin inhbits BPDE-induced damage by lowering the threshold of p53 activation
Skewis, Lynell R	1F31ES016984-01	Boston University	Bioavailibility and toxicity of engineered nanomaterials
Taylor, Tonya N	1F31ES017247-01	Emory University	Reduced vesicular catecholamine storage mediates oxidant-induced neurotoxicity
Valina-Toth, Anna Liza B	1F31ES015935-01A1	Wayne State University	Parathyroid Hormone & Vitamin D Effects on Salt Sensitivity and Vascular Function
Wilson, Shelly R	1F30ES016490-01	University Of Texas Medical Br Galveston	Ah receptor transcriptional regulation through a novel DNA binding site
Institutional Research Training Grants			
Ballatori, Nazzareno	2T32ES007026-31	University Of Rochester	Training in Environmental Toxicology
Coull, Brent A	2T32ES007142-26	Harvard University (Sch Of Public Hlth)	Graduate Training in Biostatistics
Culotta, Valeria C	2T32ES007141-26	Johns Hopkins University	Traning Program in Environmental Health Sciences
Elfarra, Adnan A	2T32ES007015-31	University Of Wisconsin Madison	Molecular & Environmental Toxicology Pre-& Postdoctoral Training Program
Guengerich, F Peter	1T35ES016534-01	Vanderbilt University	Summer Research and Training Program in Environmental Health Sciences
Hankinson, Oliver	1T32ES015457-01A1	University Of California Los Angeles	Training in Molecular Toxicology
Monks, Terrence J	1T32ES016652-01	University Of Arizona	Human Disease and the Interplay Between Genes and the Environment
Montine, Thomas J	2T32ES007032-31	University Of Washington	Environmental Pathology/Toxicology Training Program
Nebert, Daniel W	1T32ES016646-01	University Of Cincinnati	Gene-Environment Interactinos Training Program
Rice, Robert H	2T32ES007059-31	University Of California Davis	Advanced Training Environmental Health Sciences
Swenberg, James A	2T32ES007126-26	University Of North Carolina Chapel Hill	Pre- and Postdoctoral Training in Toxicology
Wessling-Resnick, Marianne	1T32ES016645-01	Harvard University (Sch Of Public Hlth)	Interdisciplinary Training in Genes and the Environment

NIEHS Awarded Competing Grants (Superfund Program) - Fiscal Year 2008

Principal Investigator	Grant Number	Grantee Institution	Project Title
Research Project Grants			
Burken, Joel G	1R01ES016158-01	University Of Missouri-Rolla	In-Situ Sediment Remediation Using Benthic Waterjet Amendment Placement
May, Harold D	1R01ES016197-01	Medical University Of South Carolina	Integrating microbial biostimulation and electrolytic aeration to degrade POPs
Sheahan, Thomas C	1R01ES016205-01	Northeastern University	A reactive mat to remediate contaminated sediments and reduce health risks
Stanton, Bruce A.	2P42ES007373-14	Dartmouth College	Toxic Metals in the Northeast: From Biological To Environmental Implications
Hennig, Bernhard	2P42ES007380-12	University Of Kentucky	Nutrition and Superfund Chemical Toxicity
SBIR/STTR Grants			
Bandera, Cesar	2R44ES014793-02	Bandemar Networks, LLC	Mobile Just-In-Time Training of Emergency Response Personnel - Phase II
Held, Christopher T.	1R44ES016670-01	Metamedia Training International, Inc.	HazMat IQ Four Step System eLearning
Held, Thomas H	2R44ES014762-02	Metamedia Training International, Inc.	Lessons Learned from Graniteville - Phase II
Hughes, Owen	2R44ES011433-02A1	Eon Corporation	Ceriodaphnia DNA Microarrays
James, Patrick I	2R44ES013622-02	Tesla Laboratories, Inc.	Advanced Toxic Metal Contaminant Remediation System
Kaye, Jonathan M	2R44ES013908-02A1	Amethyst Research , LLC	HazCommand: HazMat Incident Command Training
Kirkley, Sonny E	1R43ES016673-01	Information In Place, Inc.	Viyant Hazmat Skilled Support Personnel Just in Place Performance Support
Lee, David A	1R41ES016961-01	Edenspace Systems Corporation	Engineering Enhanced Plants for Arsenic Remediation
Mackay, Susan Gail	1R43ES016499-01	Zeomatrix, LLC	Novel Zeolite Photocatalyst for Reductive Dechlorination of Chlorinated VOCs
Willard, Dale M	1R43ES017200-01	Advanced Microlabs, LLC	Microchip-Based Perchlorate Analyzer for Water Remediation Monitoring and Field A

2009 NIEHS Biennial Advisory Council Report
Certifying Compliance with Inclusion Guidelines

Overall Assurance for Compliance with Inclusion Guidelines

The 2009 Biennial Advisory Council Report Certifying compliance with Inclusion guidelines was presented to the National Advisory Environmental Health Sciences Council on February 19.

Information Regarding Aggregate Tracking and Inclusion Data

Prior to 2002, human subjects were reported in a single table format using the following racial categories: American Indian/Alaska Native; Asian; Black or African American; Hispanic or White. Following the 2000 census, GAO changed the reporting format. Under the current guidelines, investigators are required to ask subjects to identify ethnicity and race in a two question format: ethnicity first, followed by identification of race. Although the PI is expected to collect race and ethnicity data appropriate for their particular study, they must be able to report this data in the required NIH categories. Ethnicity is broken out as either Hispanic or Not Hispanic. Race must be broken out as American Indian/Alaska Native; Asian; Black or African American; Hawaiian/Pacific Islander; or White. Subjects may identify one or more races or they may decline to identify their race. If a subject identifies as being of two or more races, the subject is reported as "More than one race." If a subject declines to identify their race, the subject is reported as "Unknown/not reported." Studies funded prior to FY 2002 may use the new method of reporting only if the information on ethnicity is available. Both formats appear in the tables in the appendix. However, the number of studies using the old format continues to decrease. In FY 2005 and FY 2006, 73.8% and 94.4%, respectively, were reported using new format. As of FY2007 NIEHS no longer has any protocols reporting using the old format.

Table 1. FY 2007 Aggregate Enrollment Data for All Extramural Research Protocols

As of data submitted in FY2007, NIEHS no longer has any extramural projects reporting through the OLD format.

New Form: Total of All Subjects Reported Using the 1997 OMB Standards

Number of Protocols with Enrollment Data: 90

	Total of All Subjects by Race								Total of All Subjects by Ethnicities			
	American Indian/ Alaska Native	Asian	Black or African American	Hawaiian/ Pacific Islander	White	More Than One Race	Unknown/ Not Reported	Total	Not Hispanic	Hispanic or Latino	Unknown/ Not Reported	Total
Female	1,103	7,876	5,599	78	21,953	1,373	1,954	39,936	33,034	5,646	1,256	39,936
	2.76%	19.72%	14.02%	0.2%	54.97%	3.44%	4.89%	58.08%	82.72%	14.14%	3.15%	58.08%
Male	780	5,739	3,085	47	15,934	1,330	1,828	28,743	23,709	4,501	533	28,743
	2.71%	19.97%	10.73%	0.16%	55.44%	4.63%	6.36%	41.8%	82.49%	15.66%	1.85%	41.8%
Unknown	16	3	9	1	17	1	38	85	27	40	18	85
	18.82%	3.53%	10.59%	1.18%	20%	1.18%	44.71%	0.12%	31.76%	47.06%	21.18%	0.12%
Total	1,899	13,618	8,693	126	37,904	2,704	3,820	68,764	56,770	10,187	1,807	68,764
	2.76%	19.8%	12.64%	0.18%	55.12%	3.93%	5.56%	100%	82.56%	14.81%	2.63%	100%

Table 2. FY 2008 Aggregate Enrollment Data for all Extramural Research Protocols

New Form: Total of All Subjects Reported Using the 1997 OMB Standards

Number of Protocols with Enrollment Data: 115

	Total of All Subjects by Race								Total of All Subjects by Ethnicities			
	American Indian/ Alaska Native	Asian	Black or African American	Hawaiian/ Pacific Islander	White	More Than One Race	Unknown/ Not Reported	Total	Not Hispanic	Hispanic or Latino	Unknown/ Not Reported	Total
Female	1,416	8,858	6,611	133	39,290	2,063	4,674	63,045	43,264	11,814	7,967	63,045
	2.25%	14.05%	10.49%	0.21%	62.32%	3.27%	7.41%	58.95%	68.62%	18.74%	12.64%	58.95%
Male	1,067	6,034	3,820	79	27,851	2,044	2,913	43,808	31,423	8,760	3,625	43,808
	2.44%	13.77%	8.72%	0.18%	63.58%	4.67%	6.65%	40.96%	71.73%	20%	8.27%	40.96%
Unknown	16	3	9	1	20	1	47	97	30	43	24	97
	16.49%	3.09%	9.28%	1.03%	20.62%	1.03%	48.45%	0.09%	30.93%	44.33%	24.74%	0.09%
Total	2,499	14,895	10,440	213	67,161	4,108	7,634	106,950	74,717	20,617	11,616	106,950
	2.34%	13.93%	9.76%	0.2%	62.8%	3.84%	7.14%	100%	69.86%	19.28%	10.86%	100%

In FY2007 the total number of clinical research protocols in which subjects were enrolled (Table 1) was 90 with a total enrollment of 68,764 subjects. Of these, 39,936 (58.08%) were female; 28,743 (41.8%) were male and 85 (0.12%) chose not to identify their gender. The racial distribution was 2.76% American Indian/Alaska Native; 19.8% Asian; 12.64% Black or African American; 0.18% Hawaiian/Pacific Islander; 55.12% White; 3.93% more than one race; and 5.56% did not identify their race. For ethnicity 82.56% were not Hispanic; 14.81% were Hispanic; and 2.63% did not report their ethnicity.

In 2008 (Table 2), there were a total of 115 research protocols with a total enrollment of 106,950 subjects. Of these, 63,045 (58.05%) were female, 43,808 (40.96%) were male, and 97 (0.09%) chose not to report their gender. The racial distribution was 2.34% American Indian/Alaska native; 13.93% Asian; 9.76% Black or African American; 0.2% Hawaiian/Pacific Islander; 62.8% White; 3.84% more than one race; and 7.14% not reported. For ethnicity 69.86% identified as Not Hispanic; 19.28% identified as Hispanic or Latino; and 10.86% did not identify their ethnicity. There is a significant increase in the number of persons not identifying their ethnicity. This appears primarily to be due to an increase in studies focused on Latino populations. In many of these studies the subjects identify themselves only as Latino. These subjects do not identify Latino as an ethnicity with a separate racial identify. As studies have moved from reporting in the old format, where Hispanic/Latino was a race, there has been a steady increase in the numbers of unknown/not reported race in Hispanic populations. NIEHS staff continues to work with principal investigators in an effort to educate them on the importance of gender and race/ethnicity reporting to minimize discrepancies due to reporting errors by principal investigators.

The enrollment numbers that are reported each year are variable as studies end and new ones begin. It is important to note there was a significant increase in the reported numbers of enrolled subjects for NIEHS between 2007 and 2008. However, this sizeable increase was seen across all of NIH between 2007 and 2008. Therefore, NIH is investigating the phenomenon. For NIEHS the increase can be explained, at least in

part, to several factors: there was an overall increase of 28% in the number of protocols reporting subject enrollment, many of these are large population-based studies and the studies that ended tended to be smaller.

NIEHS continues to have more females than males represented in research protocols. In FY2007 there were 14 studies with females only and three studies with males only. In FY2008 there were 16 female only studies and two male only studies. In addition to the increase in the number of female only and decrease in male only studies in between FY2007 and FY2008, NIEHS has several mother/child epidemiology studies, which further increases the ratio of females to males.

With the development of the new Population Tracking System, it is now possible to identify the number of research protocols that are being performed in foreign countries. In FY 2007 (Table 3) 14.4% of the protocols with enrollment take place in foreign countries. That percentage increased in FY2008 to 19.13% (Table 4).

Table 3. FY2007 - Summary of all NIEHS Extramural Clinical Research including Phase III Trials Reported: Total Number of Protocols and Enrollment by Domestic versus Foreign Protocols

PROTOCOLS REPORTED	Total All Clinical Studies*	Domestic	%	Foreign	%
Protocols with Enrollment	90	77	85.6%	13	14.4%
%	55.6%	57.5%		46.4%	
Protocols with zero enrollment. Enrollment data has not yet been submitted	72	57	79.2%	15	20.8%
	44.4%	42.5%		53.6%	
Total Number of Protocols	**162**	**134**	82.7%	**28**	17.3%
%	100.00%	100.00%		100.00%	

Table 4. FY2008 - Summary of all NIEHS Extramural Clinical Research including Phase III Trials Reported: Total Number of Protocols and Enrollment by Domestic versus Foreign Protocols

PROTOCOLS REPORTED	Total All Clinical Studies*	Domestic	%	Foreign	%
Protocols with Enrollment	115	93	80.87%	22	19.13%
%	58.97%	0.6		0.55	
Protocols with zero enrollment. Enrollment data has not yet been submitted	80	62	77.50%	18	22.50%
	41.03%	0.4		0.45	
Total Number of Protocols	**195**	**155**	79.49%	**40**	20.51%
%	100.00%	100.00%		100.00%	

NIEHS continues to have few extramurally funded Phase III trials. Our last Phase III trial with enrollment ended in FY2005. That study, which took place in Mexico, examined the effect of dietary supplements containing calcium on bone lead resorption in pregnant mothers and the blood lead levels in their babies providing the first evidence that calcium supplementation suppresses the maternal-fetus/lactating infant transfer of lead as observed in the context of a large double-blind randomized clinical trial.

In FY2008 we funded two grants that have three Phase III trials between them. The first is an intervention study in Nepal (n=4200) looking at the effect of cook stove replacement on acute respiratory illness and respiratory health of newborns and children up to 36 months of age before and after replacement. A second part of this includes the respiratory health of the intervention on family members (n=16,800) living in the same house as the children. Because this is a large study, to make sure we can adequately follow the progress of the child cohort we required the investigator report these two populations separately. Thus there are two protocols for this one grant. Because the study population is 100% Asia, there will be no analysis by race. However, the sample is sufficiently large that analysis by gender is planned.

The second study is looking at the effect of indoor particulate matter air pollution generated by wood stoves on asthmatic children in rural Montana. It is a small three-arm study: placebo control, air filters and replacement of stove with an EPA rated stove. The population in rural Montana is primarily white so again racial analysis will not be possible. Analysis by gender will take place, but the sample size may not be sufficiently large to yield significant results. Both of these grants were funded in FY2008 and will not report enrollment until FY2009.

NIEHS had no Phase III trials with enrollment in FY2007 or FY 2008. Therefore no tables for Phase III studies are provided at this time.

Strategies for Ensuring Policy Compliance with Inclusion Guidelines

In order to fulfill the congressional mandates on gender/minority tracking NIEHS extramural division has instituted procedures that are updated as necessary to ensure compliance.

It is NIEHS policy that no notice of grant award will be issued for an application that has human subjects requiring tracking unless the target and/or enrollment data have been reviewed for entry into the population tracking database.

The responsibility for compliance and tracking is vested in staff in various roles of extramural research administration. These staff members participate as appropriate throughout the process. Specifically:

- Scientific Review Administrators review coding of applications for involvement of human subjects.
- The application receives peer review with respect to meeting inclusion requirements.

- A Program Analyst reviews the tracking/inclusion information from the competing application or progress report to determine whether it is a study that requires NIH tracking or may be excepted using specific NIH guidelines; reviews for completeness and interfaces with PIs to obtain any clarification or form revisions; and forwards the data to the Health Science Administrator (HSA) for concurrence.
- The HSA reviews Analysts recommendations and reviews the projects for appropriate scientific representation of women and minorities and that the grantees are accruing a diverse population in a timely manner in accordance with their approved research plan.
- The HSA discusses any scientific issues needing further attention with the applicant.
- When the issues are resolved, the HSA forwards concurrence to the Analyst and forwards the acceptable plan to the Grants Management Specialist (GMS).
- The analyst is responsible for entering codes into the NIH grants data base; assures completeness and accuracy of the data entered; and approves the data in the tracking system.

If the study section determines a study is not in compliance with human subject's regulations or the applicant has not addressed the requirements in the application, a code is placed in the system that bars funding. Generally awards are not made until the bars-to-funding are resolved. However, it is possible to make conditional awards where no funds may be expended on human subjects research until all human subjects' issues are resolved. The bar-to-funding data can be found in Table 5.

Table 5. Extramural Research Awards: Bars-to-Funding and Resolutions

	2007	2008
Total Number of Awards	307	219
Number of Awards Involving Human Subjects	102	76
	33.2%	34.7%
Number (%) of Awards Involving Human Subjects that met the Inclusion Requirements as Submitted	102	73
	100%	96.1%
Number (%) of Awards where *Minority-Only* Bar-To-Funding was Removed by Program Staff (M_U)	0	1
	0%	1.4%
Number of Awards where *Sex/Gender-Only* Bar-To-Funding was Removed by Program Staff (G_U)	0	0
	0%	0.0%
Number (%) of Awards where both Minority AND Sex/Gender Bar-To-Funding was Removed by Program Staff	0	2
	0.0%	.2.6%
Total Number (%) of Awards where Bar-To-Funding was Removed	0	3
	0.0%	3.9%

In FY 2007, 102 of the 307 applications funded had human subjects with no application having issues that required a bar-to-funding. In FY2008, 76 of the 219 applications funded had human subjects, and 3 applications (3.9%) had issues that resulted in a bar-

to-funding. No human subjects' research was allowed to be performed until all issues were resolved and the bars were removed.

Staff Training on the Utilization of the Population Tracking System

A staff member of the Program Analysis Branch, Division of Extramural Research and Training, has been designated as the person responsible for monitoring the system and tracking as required. She has received training on the population tracking system and also participates in annual training on human subject's and bioethics-related issues through the NIH Staff Training in Extramural Programs (STEP) and other seminars. The analyst is the sole person authorized to approve data into the tracking system. She currently represents the Institute on the Gender/Minority Inclusion committee and the electronic Population Tracking Users Group and served for on the Human Subjects Protection Liaison Committee from its inception in FY2001 until its dissolution in early summer, 2008.

Additional Staff Training

NIEHS staff has participated in relevant training programs and activities including the updates offered through the Staff Training on Extramural Programs. In FY2007, the analyst responsibly for tracking inclusion, along with other Extramural staff members, completed an 8-week course on "Ethical and Regulatory Aspects of Clinical Research Training." Due to the location of the NIEHS in North Carolina, most of the staff views sessions by video-teleconference. A record of staff participation in training activities is kept through the Office of the Director of the NIEHS Division of Extramural Research and Training.

It should be noted again that this Institute has supported very few studies that would be termed Phase III clinical trials. Nevertheless, staff are expected and required to be familiar with and enforce all requirements for research involving human subjects, as defined by NIH/DHHS.

Additional information on NIH Inclusion policies, including the NIH Inclusion Committee's Comprehensive Reports can be found on the Office of Research on Women's Health at http://orwh.od.nih.gov/inclusion.html.

GENES, ENVIRONMENT AND HEALTH INITIATIVE: EXPOSURE BIOLOGY PROGRAM

EXECUTIVE SUMMARY

The Genes, Environment and Health Initiative (GEI) was established by the Department of Health and Human Services and the NIH in 2006 to lay a foundation for investigating the interaction between environmental and genetic underpinnings of human disease. The Initiative consists of two major components: identifying genetic susceptibility factors for diseases that have a high public health impact and developing new technologies for accurate measurement of environmental exposures and lifestyle factors. This four-year effort will create a capacity for further research which will lead to better predictions of disease outcomes, more precise therapies for the treatment of many illnesses, and new strategies for disease prevention.

Two GEI programs were developed to achieve these goals – the Genetics Program, led by the National Human Genome Research Institute, and the Exposure Biology Program, led by the National Institute of Environmental Health Sciences. The Genetics Program is focused on the identification of genes implicated in complex human diseases. The parallel Exposure Biology Program (EBP) will develop a set of tools for assessing individual exposure to environmental stresses including airborne chemicals, psychosocial stress, use of addictive substances, diet and physical activity as well as measures of the biological response to those stressors.

Exposure Biology Program: Overview and Scientific Progress

To determine how environmental exposures, including drug use, diet and physical activity, contribute to human disease, the EBP made 32 awards in new technologies that can accurately measure personal exposures across the spectrum from exposure to response. The products developed through these efforts will provide the improved accuracy and precision needed to determine how environmental and lifestyle factors interact with genetic factors to determine the risk of developing disease. In keeping with the developmental, capacity-building nature of the EBP, progress within the program can be seen from two standpoints: scientific progress and outreach. To date, several tangible successes have been achieved on both fronts.

Scientific progress is often quantified through an analysis of publications. Through the first year and a half of support, 7 review articles and 15 primary research articles were published by investigators in the Exposure Biology program. The BRI is the most traditional research program and as a result is the most amenable to publication; however grantees of both the chemical sensors and psychosocial stress programs have also been successful in publishing their efforts.

Perhaps a greater measure of the early success of the EBP is the effort made to translate the developmental activities into future application. Several workshops, symposia and presentations have been given to increase awareness of the program, discuss limitations

of current technologies and opportunities to address them with EBP products and to build interest from the eventual end users of these products, particularly the early adopters who are likely to be the first to applying these tools in their ongoing and planned studies. Through plenary scientific presentations featuring grantees at conferences such as the International Society of Exposure Sciences and the International Society for Environmental Epidemiology, we have worked to increase awareness of the end-user community of our efforts. Likewise, we have used more focused brainstorming sessions with a smaller group of invited participants to explore more meaningful one-on-one connections and future directions for the products of our program.

A final demonstration of the success of the EBP is the initial seeding of integration of efforts across the four component areas. Through the annual 'opportunity fund' investigators have begun to integrate capacity across the program.

Specific Program Highlights:

Sensors for Assessment of Chemical Exposures (SACE): This initiative is focused on the development of portable, self-contained, easy-to-use sensing devices that provide quantitative measures of exposure to potentially toxic airborne chemicals. The products being developed will be 'user friendly' wearable sensors that can generate quantitative, time-and-space resolved measurements of environmental exposures in the breathing zone. The eight awards made within this program include efforts to detect particulate matter, allergens, pesticides and volatile organics. Each of the projects is felt to be on-track to meet their product development milestones; some highlights and notable achievements to date include;

- NJ Tao's group at Arizona State University has completed the design of a prototype sensor array for detection of major volatile aromatic compounds including benzene-specific and total BTEX (Benzene, Toluene, Ethylbenzene and Xylene). This array has been integrated into a first generation sensor device and applied in preliminary field studies measuring environmental exposures at specific locations including campus 'hotspots', airport and gas station.

- Steve Chillrud's Group at Columbia and Pacific Northwest Labs has completed a first generation prototype with a six station filter unit for particulate and integrated GPS sensor. Extensive effort has gone into selection of components for high performance and low energy consumption. In particular, extensive testing of GPS chips for performance in 'urban canyons' was conducted to insure fast 'cold' and 'warm' starts to enable cycling of the chip and maintain optimal battery life. This unit lacks the real-time optical counter for particulate matter as well as the target 36 location sampler.

- SangYoung Son's group at the University of Cincinnati has completed most of the efforts required for miniaturization of the sampler design from the existing 1.7 kilogram unit by almost 20 fold to a final unit which will be approximately the size and weight of a cell phone and which will enable real time detection of

particulate matter from 10 nm to 1 micron. The prototypes will be tested in an existing children's asthma cohort NIEHS supports in Cincinnati during the fourth year of the project.

Improved Measures of Diet and Physical Activity (DPA): This initiative, led by the National Cancer Institute and National Heart, Lung and Blood Institute, is promoting the development of reliable and economically feasible technologies for accurate measurements of diet and physical activity and, in general measures of total energy expenditure, either individually or in an integrated package. These efforts include three projects focused exclusively on developing direct measures of physical activity and analysis of activity patterns, three projects focused on camera-based analysis of dietary intake and improved 24 hour recall assessments, and one project focused on integrating both diet and physical activity assessments into a single device. Highlights of this effort to date include:

- Calculation of food volume to estimate portion size from images of foods taken with mobile phones is progressing well—several factors affect accuracy and most are controllable.

- A series of papers describing the diet projects are drafted and will be submitted for publication in a Journal of American Dietetic Association special issue on assessment methods

- Significant progress made on integration of accelerometers with mobile phones and real-time recognition of different types of physical activity using multiple sensors.

- Working Group meeting planned for July, 2009 to bring together experts to define best practices for calibration and validation of activity monitors. This meeting is co-sponsored by NHLBI, NCI, GEI, and the American College of Sports Medicine (ACSM).

Network for Quantifying Exposures to Psychosocial Stress and Addictive Substances (NEPSAS): This initiative, led by the National Institute on Drug Abuse, is targeting the development of measurement technologies that can improve detection and quantify personal exposure to psychosocial stress and/or addictive substances. Psychosocial stressors include acute events like daily stresses and traumatic events, as well as chronic events such as crowding or isolation, discrimination, or family violence. The awards issued through the NEPSAS program include a combination of ecological momentary assessment and biological measures of stress and addictive substance use. Highlights from this effort to date include:

- Vivek Shetty's group has produced a 2nd generation portable biosensor with field deployable features. This sensor system uses a colorimetric 'dipstick' approach to detect salivary alpha amylase rapidly and with minimal user action.

- Mark Rea's group has developed a phasor analysis for assessing circadian entrainment to the light-dark cycle. This new method quantifies, in a simple, robust way how well people respond to the environmental light-dark pattern. They have published a description of this technique this year in the *Journal of Circadian Rhythms.* Of note, the paper is already number 8, all time, on the list of most accessed papers from that journal.

- Santosh Kumar's team has developed a skin-patch sensor system with embedded micro-processors and wireless transceivers that will enable simultaneous measurement of stress markers and alcohol within the field without requiring active participation from subjects. Their measure of alcohol is an interstitial-fluid (ISF) based sensor that is strapped on the arm; their physiological stress measurements are composed of several sensors strapped on a chest band which measures skin conductance, heart rate, respiratory rate, temperature and physical activity.

Biological Response Indicators of Environmental Stress (BRI): This initiative focuses on the development of robust biomarkers for detecting subtle changes in biological systems following exposure to environmental stressors. These biomarkers reflect changes in key biological pathways, such as inflammation, oxidative stress, DNA damage, endocrine disruption, immune activation and epigenetic regulation, which are known to be influenced by environmental stressors and are linked to the pathogenesis of common diseases. Twelve awards were issued through the BRI program including two centers, which include an additional element of biosensor development in addition to the biomarker discovery activities. Highlights of this program to date include:

- Tim Huang's group at Ohio State University is studying persistent global methylation patterns in breast stem progenitor and breast tumor cells following exposure to xenoestrogens (e.g., DES, 17β-estradiol, and daidzein). Their hypothesis is that methylation patterns serve as a "molecular relic" of prior exposure. Early results from massive parallel sequencing efforts suggest clusters of hyper-methylation in selected areas of genome suggesting coordinate methylation and gene silencing with xenoestrogen exposure.

- Avi Spira at Boston University is developing gene expression signatures as biomarkers of host response to tobacco smoke in bronchial, nasal and buccal epithelium. Early comparisons of patterns from cells from bronchial brushings show that nasal epithelium patterns correlate well with those of bronchial epithelium.

- Yuehe Lin from the U54 Center at PNNL has developed a prototype biosensor for detecting cotinine, nitrated proteins and other protein modifications that result from obesity and cigarette smoke-induced oxidative and inflammatory stress. The biosensor is an ELISA-type device that uses nanoparticle-conjugated antibodies to enhance signal from binding by cotinine or nitrated proteins. The cotinine assay is based on competitive binding using a simple absorption pad, a QD-labeled

cotinine conjugate and a secondary anti-cotinine antibody. The prototype has been tested successfully with cotinine and nitrated fibrinogen (as a general biomarker of inflammation) and will be tested with other modified proteins identified in projects 1 and 2.

- Rich Mathies lab at UC Berkeley has developed a single cell genetic analysis method that can be used to sequence DNA and PCR-amplify targets in single cells. The method relies on the generation of uniform nanoliter emulsion droplets that contain (statistically) a single cell's worth of DNA, reverse primer beads and dye-labeled forward primers (see slide).

Opportunity Fund: From the beginning of the Exposure Biology Program, it was felt that the investigators needed to have a high degree of freedom to conduct their studies: to capitalize on opportunities to meet their product development goals faster, to add new capabilities to their products, to integrate the efforts of others into their products or to explore future directions to advance the goals of the EBP. Therefore, an annual pool of $1 million was established for a supplement program to advance the goals of the EBP and improve the quality and capability of the products we will be developing. These funds have gone to purchase new equipment, to support new research directions, to support cross-grantee and cross-program collaborations and to hold workshops to strengthen the EBP effort. Highlights of the 2008 opportunity fund include:

- A collaboration between investigators in the Chemical Sensors program (Chillrud and Rodes) and Physical Activity program (Initille, Raab, and Haskell) to integrate accelerometers and activity analysis into particulate matter sensors to inform not only about subject compliance but also to add potential analysis on commuter behavior and correlations between activity and exposure underlying an adverse response.

- A research supplement to Spira's group has begun studying effects of tobacco smoke exposure on microRNA expression. A recently published PNAS paper supported by this effort shows a clear negative correlation between increased gene expression and decreased MAGF expression (transcription factor found to be differentially expressed in smokers) with smoking.

- An opportunity fund supported collaboration between Vivek Shetty (NEPSAS) and Ashok Mulchandani (SACE) has established proof of principle that functionalized nanowires can be used as multiplexed biosensing platforms for measuring larger panels of salivary stress indicators.

- Investigators from 9 of the GEI funded projects (DPA, NEPSAS and SACE) will come together to share experiences with and plans for the use of Global Positioning System (GPS) and Geographical Information Systems (GIS) data in their research. The aim is to begin dialogue on the potential for common measures, analytical strategies and outputs from the overall GEI initiative.

GEI Future Directions

The intent of the GEI was to use the initial four year funding period, from 2007 to 2011, to establish a capacity in tools, methods and expertise which could then be applied in population based studies to understand the interaction between genetic and environmental factors. Both programs are well on their way to achieving those goals. We are, however, faced with a reality that progressing with this vision will be cost-prohibitive in the current fiscal environment. A second reality is that while progress on EBP product development is proceeding very rapidly, acceptance of these tools by the end user community will require a level of validation and commercialization that was never intended to be supported in the current GEI activities.

The ideal next step would be a continuation of the GEI effort focused on establishing a population-based proof of principle that integrates measures of exposure and genetic variation can allow testing of additional hypotheses and the generation of improved understanding of the disease process and susceptibility. To make this feasible, it would be best to target this to a particular area, such as asthma, where there is sufficient evidence that both genetic and environmental factors contribute and there is sufficient targeted tool development proceeding in the EBP to strengthen the definition of exposure.